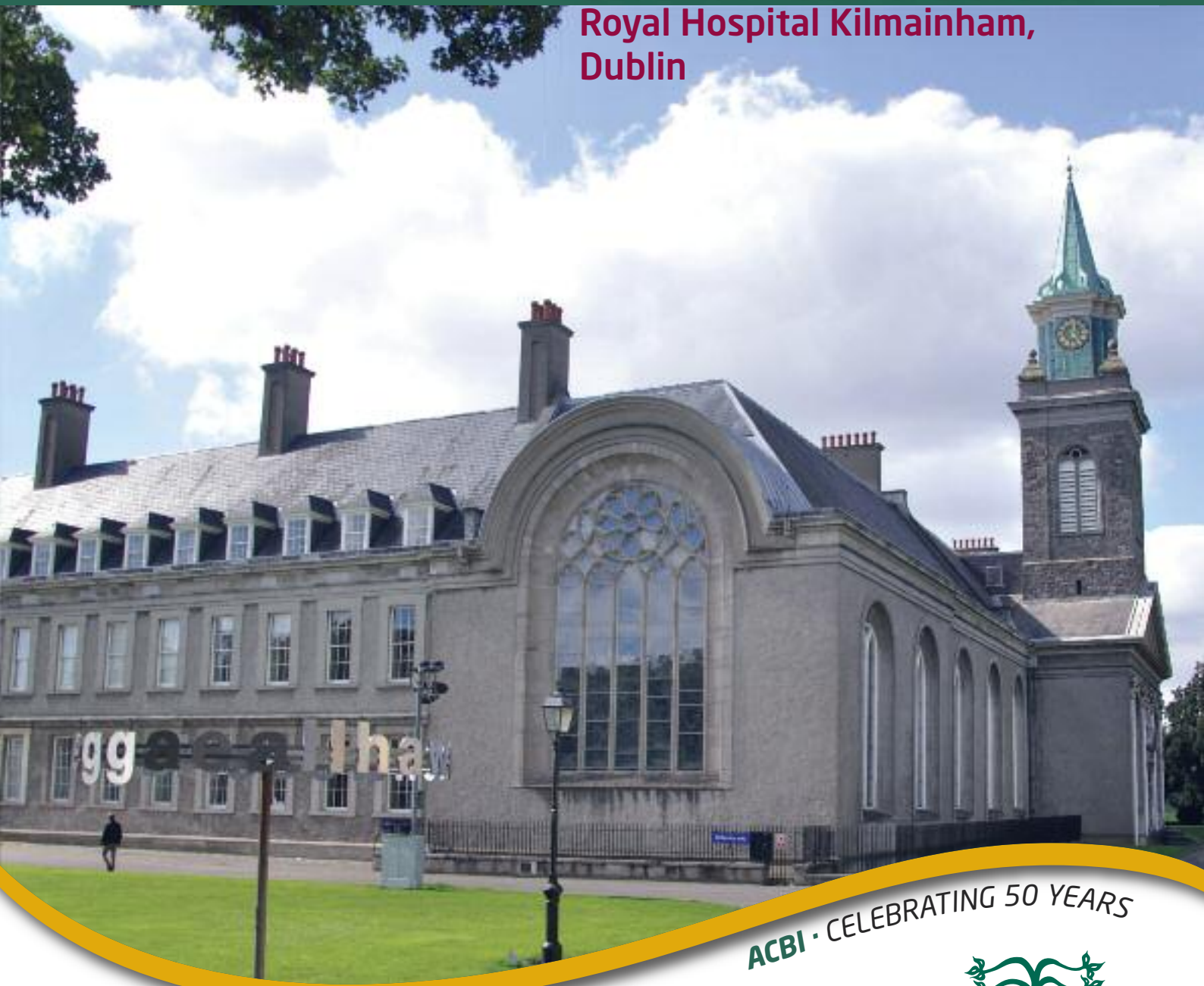


Proceedings of 37TH Annual Conference

Association of Clinical Biochemists in Ireland

**Royal Hospital Kilmainham,
Dublin**



Friday & Saturday,
November 14th & 15th

2014

ACBI • CELEBRATING 50 YEARS



ISSN: 1649-7651



Proceedings of
37TH Annual Conference
Association of Clinical Biochemists in Ireland

**Royal Hospital Kilmainham
Dublin**

November 14-15, 2014



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Royal Hospital Kilmainham · through the Window

A message from the President of the ACBI

On behalf of the Association of Clinical Biochemists in Ireland (ACBI), it is with great excitement that I welcome delegates to the 37th Annual Conference on this the 50th Anniversary of the Association. Coincidentally, the conference venue, the Royal Hospital Kilmainham built by Sir William Robinson in 1684, celebrates its 330th anniversary! Do we dare hope?

This year's conference topics are varied and wide ranging and include translating data and research into health outcomes, inflammatory disease, Vitamin D as an anti-inflammatory therapy, the clinical application and quality of next generation sequencing technology and human metabolic disease. These topics will give a flavour of the major advances being made in the discipline. In addition we will have some fascinating clinical cases and some personal reflections on a career in Clinical Biochemistry.

Poster presentations are a means for delegates to showcase research and innovation and we are delighted that significant numbers of posters have once again been submitted to the conference. The Geraldine Roberts Medal will be awarded for best scientific poster.

Royal Hospital Kilmainham · through the Grounds

The social aspect of the conference must not be overlooked. It provides for catch-up with colleagues and friends, and affords the opportunity to network and brainstorm in a pleasant atmosphere. A highlight of the year is the Annual Dinner of the Association and 2014 should prove to be no exception. This year the dinner marks a special occasion, the founding of the Association 50 years ago. Music on the night is provided by the highly regarded Astral String Quartet.

A special thank you must go to the diagnostics industry for their generous and sustained support of the Annual ACBI Conference. Dr Martin Healy (Chair of the conference committee) and the committee members of St James's Hospital and the Coombe Women & Infants University Hospital, in particular must be congratulated for their dedication and hard work in organising such a comprehensive and stimulating scientific programme. Finally, I would like to thank you the delegate for your participation and support of the conference and to wish one and all a very enjoyable and productive meeting on this the 50th year of the ACBI.

Paula O'Shea
President, ACBI



Welcome ACBI 2014

I am delighted to welcome you to the 37th Annual Conference of the Association of Clinical Biochemists in Ireland (ACBI). 2014 also marks the 50th Anniversary of the establishment of the Association.

The meeting this year will be held for the first time in the magnificent surroundings of the Royal Hospital Kilmainham, Dublin. This faithfully restored 17th century building is, architecturally, one of a few of its kind in the world and is modelled on Les Invalides in Paris. The Royal Hospital in Chelsea, London, is similar in style.

We have assembled a host of top quality speakers from Ireland and abroad for you with lectures on translational medicine and health informatics, inflammatory bowel disease and genetics. To mark the 50th anniversary of the founding of the ACBI a personal perspective will be given on the changes in clinical biochemistry over the last number of years. May I take this opportunity to thank all of our speakers who have given so freely of their time and to the chairpersons for guiding the sessions along.

As in the past we have a varied and interesting collection of poster presentations which I encourage you to view. Thanks to all those who took the time to submit their work. The Geraldine Roberts medal will be awarded to the poster deemed best overall by an independent panel of judges.

It goes without saying that a conference like this would be difficult to organise without the help of our corporate colleagues. Since its inception they have continued to back us. Their on-going support is much appreciated.

Of course, without you the delegates there would be no conference. I thank you for your participation, now and in the past, and encourage you to tell us what you think and what you would like to see in future events. At the end of the conference please take time to fill out the evaluation forms.

Organising a meeting such as this is a team effort and this year has been no exception. My thanks go to the conference committee which consisted of members from St. James's Hospital and the Coombe Women & Infants University Hospital. They worked long and hard to ensure the success of ACBI 2014.

Martin Healy

Chairman ACBI 2014 Organising Committee

Royal Hospital Kilmainham · Quadrangle



Royal College of Pathologists

ACBI 2014 Conference has been approved for CPD by the Royal College of Pathologists.

The maximum credits awarded are 9 points for the two day conference.

In order to receive these credits, the participant must sign the RCPATH register for each day attended and is issued with a certificate of attendance by the conference organising committee.

Academy of Medical Laboratory Sciences

This meeting is accredited with 5 CPD points per day and is not password protected.

For AMLS member's to get points log on to the AMLS website and for:

Attendance one day: Select Continuing Education, National/International conference 1 day = 5 points, and upload attendance certificate.

Attending both days: Select Continuing Education, National/International conference 2 days = 10 points, and upload attendance certificate.

Each member is issued a certificate of attendance by the conference organising committee.

ACBI CPD Scheme

Following a successful pilot scheme, the ACBI is introducing a CPD scheme for its members. Initially, the cost of the scheme will be included in the annual ACBI membership fee.

The facility to collate your personal CPD will be available on the members' area of the ACBI website.

At this year's Annual Conference Dermot Deverell, ACBI Webmaster, will demonstrate how to input CPD details into the ACBI website.

Evaluation of ACBI 2014

All conference participants are requested to complete the conference evaluation form located in the delegate bags. This form is to be returned to the conference registration desk.

Royal Hospital Kilmainham · Great Hall



Acknowledgements

The Organising Committee for ACBI 2014 gratefully acknowledge the very generous support of the following:

Major Sponsors:



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ACBI 2014 was jointly organised by members from St. James's Hospital Dublin and The Coombe Women & Infants University Hospital Dublin

St. James's Hospital, Dublin

Chairman: Dr. Martin Healy

Dr. Alan Balfe

Dr. Barbara MacNamara

Coombe Women & Infants University Hospital

Ruth O'Kelly

Mary Stapleton

Treasurer

Paddy Quigley

Thanks also to:

Webmaster: Dermot Deverell

Conference Photographer: Peadar McGing

Caterers: Brambles (Maeve Reid)

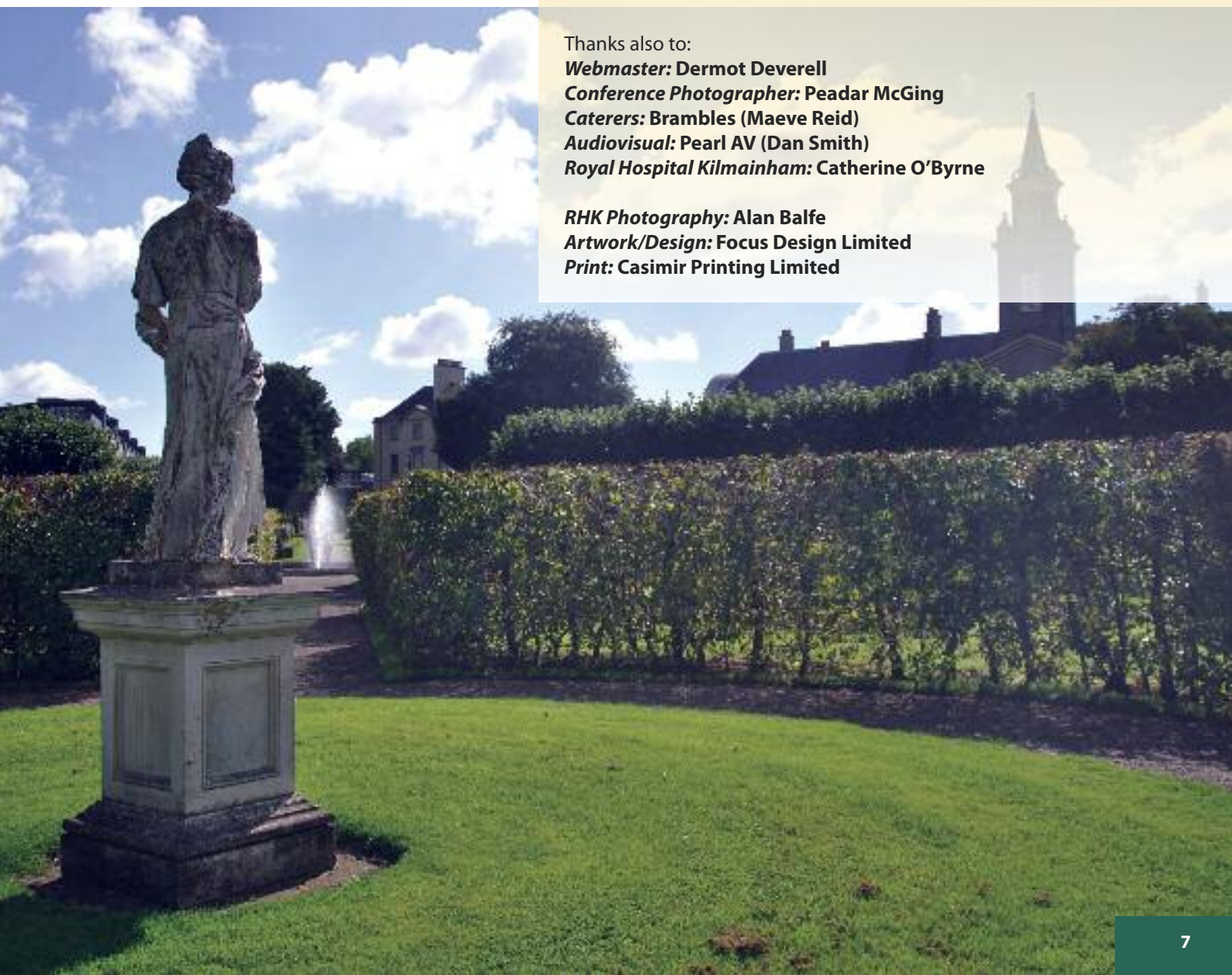
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Friday 14 November 2014

09:00-10:00: Registration. Tea/Coffee/Light Refreshments

Conference Opening

10:00-10:15: **Ms. Paula O'Shea**, President of the ACBI
Opening Remarks

10:15-10:45: **Professor William Reville**,
Emeritus Professor of Biochemistry and Public Awareness of Science Officer at
University College Cork
Science and Society

Session 1 Friday Morning

TRANSLATING DATA AND RESEARCH INTO HEALTH OUTCOMES

Chair: **Dr. Damian Griffin**, Consultant Chemical Pathologist, Galway University Hospital

10:45-11:30: **Prof. Jonathan Kay**,
Nuffield Department of Clinical Laboratory Sciences, University of Oxford
Reusing Laboratory Data to Improve the Health of the Population

11:30-11:50: Tea/Coffee/Biscuits & Poster Viewing **Sponsored by** 

11:50-12:35: **Prof. A Neil Turner**,
Professor of Nephrology, University of Edinburgh
10 Years of Giving Patients Live Access to Results – PatientView

12:35-13:20: **Prof. John V. Reynolds**,
Department of Surgery, Trinity Centre for Health Sciences, Trinity College Dublin,
and St. James's Hospital, Dublin
Surgery at the Translational Interface in Cancer Research

13:20-14:30: Buffet Lunch

Session 2 Friday Afternoon

INFLAMMATION: LABORATORY AND CLINICAL ASPECTS

Sponsored by



Chair: **Dr. Vivion Crowley**,
Consultant Chemical Pathologist, St. James's Hospital, Dublin

14:30-15:15: **Prof. Fergus Shanahan**,
Professor of Medicine and Director Alimentary Pharmabiotic Centre,
University College Cork
The Microbiome – Lessons Learned

15:15-16:00: **Prof. Maria O'Sullivan**, Professor in Human Nutrition,
Trinity Centre for Health Science, St James's Hospital, Dublin
**Vitamin D as an Anti-inflammatory Therapy in Inflammatory Bowel Disease –
New Hope or False Dawn?**

16:00-16:45: **Prof. Roy Sherwood**,
Consultant Clinical Scientist & Scientific Director, Viapath, King's College Hospital
and Professor of Clinical Biochemistry, King's College London
Biomarkers in the Diagnosis and Management of Inflammatory Bowel Disease

16:45-17:15: Tea/Coffee/Biscuits & Poster Viewing

17:15-17:45: Guided Tour of RHK Buildings

Friday Evening November

19:15: **Wine Reception in RHK**
(Classical music provided by Astral String Quartet)

20:00-late: **Annual Dinner and Musical Entertainment in RHK**
(Astral String Quartet – from Baroque to Rock)

Sponsored by



Saturday 15 November 2014

Session 3 Saturday Morning

09:00-10:00 ACBI AGM (Ordinary Members only)

10:00-10:30 Tea/Coffee/Light Refreshments

GENETICS: LABORATORY ASPECTS AND CLINICAL BREAKTHROUGHS

Chair: **Ms. Caroline Joyce,**
Principal Clinical Biochemist, Cork University Hospital

10:30-11:15: **Dr. Derek Morris,**
Co-Director, CogGene Group, National University of Ireland, Galway
Next Generation Sequencing: Applications and Challenges in the Clinic

11:15-12:00: **Dr. Michael Morris,**
Director, Department of Molecular Diagnostics, synlab, Lausanne, Switzerland
How can we Assure the Quality of Genetic Tests?

12:00-12:45: **Prof. Sir Stephen O'Rahilly,**
Professor of Clinical Biochemistry and Medicine, University of Cambridge
Human Metabolic Disease: Lessons from the Extremes

12:45-13:45: Buffet Lunch

13:45-14:15: Judges Poster Tour

Session 4 Saturday Afternoon

CLINICAL CASES/GUEST LECTURE/POSTER PRIZE

Chair: **Dr. Ned Barrett,**
Retired Consultant Clinical Biochemist, University Hospital, Limerick

14:20-14:40: **Ms. Caroline Joyce,**
Principal Clinical Biochemist, Cork University Hospital
Unravelling a Case of Neonatal Diabetes

14:40-15:00: **Ms. Deirdre Deverell,**
Principal Clinical Biochemist, Temple Street Children's University Hospital, Dublin
Molybdenum Cofactor Deficiency – Diagnostic Pitfalls on Day 2 of Life

15:00-15:45: **Dr. Pooler Archbold,**
Retired Consultant Chemical Pathologist,
Belfast City Hospitals Trust, Northern Ireland
Clinical Biochemistry – a Personal Perspective

15:45-15:55: Presentation of Geraldine Roberts Medal for best scientific poster

16:00: Conference close

16:00-17:30: IMMA Exhibition Gallery open

MedLab Pathology – 1st Irish Laboratory Accredited to ISO 15189:2012

On 31 July 2014, MedLab Pathology became the **first Irish Laboratory** to receive approval from INAB for accreditation to the **ISO 15189:2012** standard for the scope cited in 296MT. The May assessment visit was the most recent in the 3-year relationship MLP has with INAB, beginning with the accreditation requirement to repatriate the national cervical screening programme sample analysis back to Ireland in 2011.

Since then, MedLab Pathology has offered accredited testing in Chemistry, Haematology and Molecular Biology, with a current project for Microbiology accreditation underway. It is an exciting time here in Ireland, with both public and private clinical laboratories all moving towards ISO 15189:2012, since the departure of the CPA standards in 2013. Accreditation in ISO 15189 has been available to Irish Laboratories from INAB since 2003 and with the publication of the latest version of the standard in November 2012, coupled with the departure of CPA, laboratories have been in planning & transition mode since.

Here at MLP, we take quality seriously – in addition to our dedicated QA department, we cross train QA Representatives in each department to perform QA Audits, review QA documentation and participate in Continuous Improvement projects. Our leadership is focused on patient-centred healthcare, providing accurate and relevant information to all of our clients. We look forward to expanding our accredited test menu and continuing to collaborate with all of our clients.

Interested in **Quality Assurance Consultancy Services**, please contact us on 01 2933690 or email mlpqualityassurance@medlabpathology.ie

MedLab Pathology (MLP) Providing You With A First Class Pathology Testing Service

MLP is accredited to the **ISO 15189:2012** medical testing standard, we offer comprehensive multi-disciplinary pathology services to GP's and hospitals throughout Ireland. MLP was established in May 2010 as Sonic Healthcare's Irish laboratory facility. MLP has been developed to bring together Sonic Healthcare's proven international capabilities and local expertise to provide internationally recognised best practice developments in laboratory medicine. We are committed to delivering service excellence through our dedicated clinical, scientific, customer service and logistics staff.

May 2010
MLP awarded National
Tender for Cervical
Cytology Screening

December 2011
Award of
ISO 15189:2007
accreditation for
Cytology

June 2012
Accreditation awarded
for HPV

October 2012
Extension to
ISO 15189:2007
scope for Haematology
& Chemistry awarded

July 2014
Accreditation to the
ISO 15189:2012
standard awarded
& extension to
scope for Malaria
Parasites

August 2010
MLP Opens

May 2012
MLP awarded sole
laboratory provider for
National Colon Cancer
Screening Tender

August 2012
Accreditation awarded
for HPV on the
Roche 4800

June 2013
Extension to scope
awarded for Coagulation
& FIT analysis

For More Information

If you would like more information on MLP's services please contact our Sales Department on sales@medlabpathology.ie or 01 2933690



Session 1

TRANSLATING DATA AND RESEARCH INTO HEALTH OUTCOMES

Chair:

Dr. Damian Griffin, Consultant Chemical Pathologist,
Galway University Hospital

Prof. Jonathan Kay

Nuffield Department of Clinical Laboratory Sciences,
University of Oxford

**Reusing Laboratory Data to Improve the Health
of the Population**

Royal Hospital Kilmainham · through the Gate

Prof. A Neil Turner

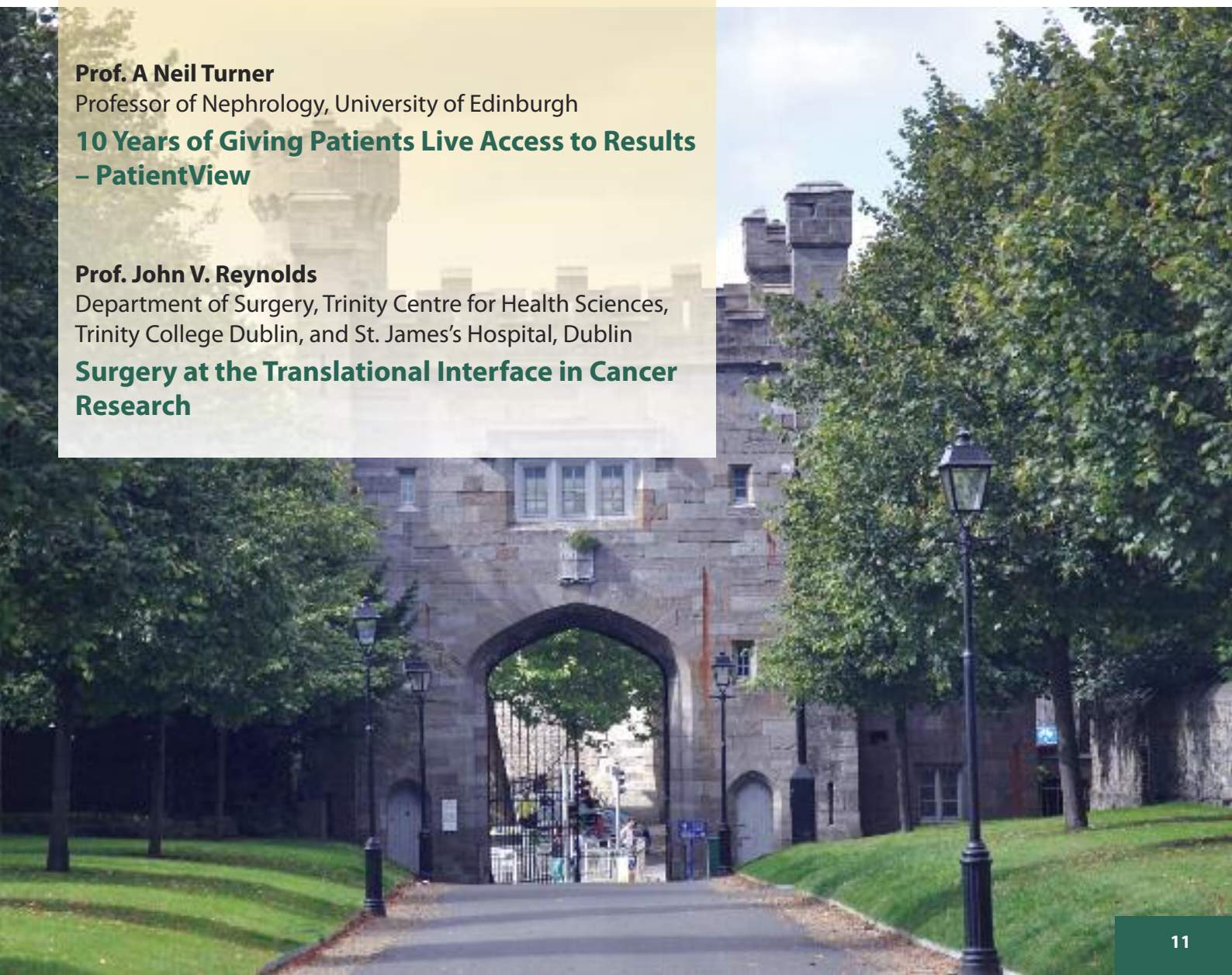
Professor of Nephrology, University of Edinburgh

**10 Years of Giving Patients Live Access to Results
– PatientView**

Prof. John V. Reynolds

Department of Surgery, Trinity Centre for Health Sciences,
Trinity College Dublin, and St. James's Hospital, Dublin

**Surgery at the Translational Interface in Cancer
Research**



Session 1

Professor Jonathan Kay
Nuffield Department of Clinical
Laboratory Sciences,
University of Oxford

BIOGRAPHY

Health Informatics at the Centre for Health Informatics, City University London and was a Consultant Chemical Pathologist at the Oxford Radcliffe Hospitals for 30 years. He has been Chairman of the Information Group of the Academy of Medical Royal Colleges and was a senior consultant to the Design Authority of the NHS National Programme for IT for England.

For many years he has been trying to derive clinical benefits by persuading computers to communicate. This has included work on automated transmission of laboratory reports to general practitioners, hypertext advisory systems and handheld wireless computers. With his colleagues John McVittie, David Nurse and Christos Bountis he has won six national and international awards, including the 1998 Deloitte Consulting Award for Information Management Project of the Year and a 2003 European Union Best Practice in eHealth Award for the development of the Oxford Clinical Intranet.

His work with Professor Mike Murphy on improvements to blood transfusion won the 2012 HSJ Award for "Improving Care with Technology" and the 2012 National Patient Safety Award for "Technology and IT to improve Patient Safety".

He is a Board Member with responsibility for patient liaison of "Lab Tests Online UK", a patient-facing website about laboratory investigations.

Professor Kay enjoys human powered vehicles, driving the Caterham 7 which he built, and acting with the Garsington Players.

Reusing Laboratory Data to Improve the Health of the Population

The primary function of laboratory medicine is to get information about an individual patient to the right clinician at the right time. But there are also many secondary functions where we are familiar with using data aggregated across patients. These include analysis of workload, reimbursement, quality management and method assessment.

"Big data" has been used in epidemiology for many years, but a combination of pressures and opportunities have created enormous recent attention. The pressures include the repeated rediscovery that much more prevention is needed to improve the population's health and the need to spend less on interventional healthcare. The opportunities include cheap computation, better visualisation tools, geographical information systems and the experience of other domains such as retail.

Longitudinal studies of a population using laboratory data alone can provide new insights into both the burden of disease and the current provision of healthcare, and when combined with clinical and demographic data will support improvements in the planning and delivery of healthcare, the generation of new knowledge and patient empowerment.

Session 1

10 Years of Giving Patients Live Access to Results – PatientView

The PatientView project was initiated as a pilot to test showing results to patients online in four renal units in 2004. It took feeds from renal unit systems and presented live results along with information about the tests, treatments, and clinical correspondence. These were very well received, without the negative effects some feared, and since then the system has extended to include renal units covering 90% of the UK population, with take-up of over 60% in some patient populations. Patient responses are very strongly positive, but strikingly, after a time so too are staff responses. It is funded by subscriptions from units offering it.

Regular users (about 60% of the total, but apparently rising) log in a median of twice each month. The age difference between users and non-users has narrowed to 3 years. Most logins are around new results, or more broadly around visits. Most requests are to include more information. Recently the system has been adapted for two additional specialties and to permit two-way interaction with patients, including pilots of secure messaging. From Jan 2015 a modified 'PV2' will increase adaptability for different specialties, open up possibilities for new ways of working, and be much more friendly to mobile devices.

Professor Neil Turner
*Professor of Nephrology,
University of Edinburgh,
Scotland*

BIOGRAPHY

Neil Turner is Professor of Nephrology at the University of Edinburgh and a consultant nephrologist with particular clinical interests in autoimmunity, genetic diseases and in paediatric-adult transition.

A background in molecular research as a clinical academic led to progressive involvement in a number of educational and information projects, including resources for staff but notably also patient information. In 2004 he became involved in the initiation of the Renal PatientView project, for which he leads the steering group. This now gives over 35,000 patients online access to live test results and information about their disease and treatment, including now specialties beyond Renal.

He has a major role in undergraduate medical education in Edinburgh and is involved in various international educational activities through the International Society of Nephrology and Scottish Government-Malawi projects. In 2011 he founded an online postgraduate MSc in Internal Medicine in collaboration with the Royal College of Physicians of Edinburgh. He is an author or editor for several nephrology textbooks.

Session 1

Professor John V. Reynolds
*Department of Surgery,
Trinity Centre for Health Sciences,
Trinity College Dublin, and
St. James's Hospital, Dublin*

BIOGRAPHY

Professor Reynolds is Professor of Clinical Surgery at the St. James's Hospital and Trinity College Dublin. He is the National Lead for oesophageal and gastric cancer. He is Cancer Lead at St. James's Hospital and the Trinity School of Medicine, and a Principal Investigator in the Trinity Translational Medicine Institute. He has formerly held Fellowship positions with the University of Pennsylvania and Wistar Institute in Philadelphia and at the Memorial Sloan-Kettering Cancer Centre in New York. He was a Senior Lecturer at St. James's University Hospital in Leeds (1994-6)

Professor Reynolds has obtained numerous research awards and has published widely in cancer research, with over 250 publications and approximately €5m research grant income. His clinical interest is in diseases of the oesophagus and stomach. His research interest is in four areas: (1) pathogenesis of Barrett's oesophagus and progression; (2) prediction of response and resistance to chemotherapy and radiation therapy; (3) obesity, altered metabolism, and cancer; (4) malnutrition and peri-operative nutrition.

Surgery at the Translational Interface in Cancer Research

Cancer surgery has evolved significantly over the last 25-30 years. Notable among significant progress are overall improved oncological outcomes, a safer patient journey, optimisation of staging and treatment pathways, surgery for metastatic disease, and the introduction of modern technologies, in particular minimally invasive approaches. Internationally, surgeon scientists within broad based interdisciplinary programmes have also contributed enormously to cancer research discovery over this period. In this presentation, the key elements of such progress will be discussed.

The current focus of the translational programme within the Department of Surgery at the Institute of Molecular Medicine, TCD, will also be presented. This includes platforms in the following:

- (1) determining factors predicting response or resistance to chemotherapy and radiation therapy in gastrointestinal cancer;
- (2) the role of visceral obesity and metabolic syndrome in cancer risk;
- (3) inflammation to cancer pathways in the upper gastrointestinal tract; and
- (4) clinical and translational trials.

Session 2

INFLAMMATION: LABORATORY AND CLINICAL ASPECTS

Chair:

Dr. Vivion Crowley

Consultant Chemical Pathologist,
St. James's Hospital, Dublin

Prof. Fergus Shanahan

Professor of Medicine and Director Alimentary Pharmabiotic
Centre, University College Cork

The Microbiome – Lessons Learned

Prof. Maria O'Sullivan

Professor in Human Nutrition,
Trinity Centre for Health Science, St James's Hospital, Dublin

Vitamin D as an Anti-inflammatory Therapy in Inflammatory Bowel Disease – New Hope or False Dawn?

Prof. Roy Sherwood

Consultant Clinical Scientist & Scientific Director, Viapath,
King's College Hospital and Professor of Clinical Biochemistry,
King's College London

Biomarkers in the Diagnosis and Management of Inflammatory Bowel Disease

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Royal Hospital Kilmainham · Garden



Session 2

Professor Fergus Shanahan
Alimentary Pharmabiotic Centre,
University College Cork

BIOGRAPHY

Fergus Shanahan MD, DSc is Professor and Chair of the Department of Medicine, University College Cork, National University of Ireland, and Director of the Alimentary Pharmabiotic Centre, a research centre funded by Science Foundation Ireland which investigates host-microbe interactions in the gut and the therapeutic potential of mining the microbiota. His interests include most things that affect the human experience. He has published over 460 scientific articles and several books in the areas of mucosal immunology, inflammatory bowel disease and the microbiota and including several articles relating to the medical humanities.

The Microbiome – Lessons Learned

Mankind has used microbes to do everything from cleaning up oil slicks to making life-sustaining drugs. Humans have evolved over millennia with microbes which are critical for optimal development and health maintenance. The digestive tract is the most densely populated ecosystem on earth, containing more bacteria than mammalian cells in the body and more microbial genes (microbiome) than the entire human genome. This living inner biomass is a rich repository of metabolic signals that is tantamount to a hidden inner organ with an activity rivalling that of the liver. Signals from this inner microbial world are required for development not only of the digestive tract but also for development and education of the immune system. Disturbances of immune function and chronic inflammatory or allergic disorders are increasing in frequency in modern society and these disorders have been linked with the features of the modern lifestyle of developed countries. Many of the features of a modern lifestyle such as sanitation, urbanisation, antibiotic usage, vaccination, reduced family size, high fat diets, lack of exercise and even obesity, can be related to changes in the composition of the human gut microbiota. Mechanisms relating the intestinal bacteria with health and disease are emerging and recent advances in technology have eliminated many of the obstacles to studying the microbiota and its mysteries. There is now the very real prospect of bio-prospecting in the gut, whereby the microbiota can be therapeutically manipulated or 'mined' for the next generation of drugs ranging from novel anti-microbials to anti-inflammatories. This 'bugs to drug' programme of discovery is already underway and paying dividends. It offers a new challenge for both the functional food and pharmaceutical sectors of industry in partnership with academia.

Session 2

Vitamin D as an Anti-inflammatory Therapy in Inflammatory Bowel Disease – New Hope or False Dawn?

There is increasing scientific interest in the field of vitamin D research, moving the focus beyond bone health to other disease processes. Low circulating vitamin D levels have been reported as a risk factor for several pathophysiologically divergent diseases including cancers, diabetes, cardiovascular diseases, multiple sclerosis and inflammatory diseases including rheumatoid arthritis and inflammatory bowel disease (IBD). But, can any single nutrient contribute to multiple complex disease mechanisms and, ultimately, have therapeutic potential?

The aim of this presentation is to critically evaluate several strands of scientific evidence surrounding vitamin D and inflammation in IBD. Epidemiological studies suggest an increased incidence of IBD in countries of more Northern latitudes, mirroring sunlight patterns and vitamin D status. A considerable body of evidence supports the anti-inflammatory effects of vitamin D, at least in animal models of IBD. While it is accepted that suboptimal vitamin D status is common in IBD, some studies propose that this correlates with, and contributes to, more severe disease. Nevertheless, in this context, reverse-causality must be considered. With regard to treatment, evidence is only beginning to emerge from randomised controlled trials (RCTs) to suggest that people with IBD may remain in remission longer when treated with oral vitamin D. In conclusion, several strands of evidence suggest that vitamin D may modify the immune response in IBD. However, there is a continued need for large well-designed clinical trials and mechanistic studies to determine if this emerging promise for vitamin D translates into tangible clinical benefits for people with IBD.

Professor Maria O'Sullivan
*Professor in Human Nutrition,
Trinity Centre for Health Science,
St. James's Hospital, Dublin 8*

BIOGRAPHY

Maria O'Sullivan is Associate Professor in Human Nutrition at Trinity College Dublin. As a Principal Investigator, her research focuses on the role of nutrition in inflammation, in particular vitamin D in the initiation and treatment of inflammatory diseases. In 2013, she became the first Irish recipient of the Nutrition Society's Cuthbertson Medal, awarded in London, in recognition of research that translates to patient care. Currently, she is Editor-in-Chief of the journal 'Proceedings of the Nutrition Society'. Maria has several roles in committees and societies including the Nutrition Society and the Royal Irish Academy.

Maria's research is supported through competitive government grants, including a large HEA consortium grant, the Irish Research Council, non-profit organizations and an EU COST action network. Maria has published and presented original research extensively in Europe and North America as well as invited lectures and co-chairs. She has in excess of 125 publications, with 40 full papers. She has extensively reviewed for journals and grant bodies, including the European Commission (Brussels) and the US Department of Defense (Washington). maria.osullivan@tcd.ie

Session 2

Professor Roy Sherwood
Consultant Clinical Scientist &
Scientific Director, Viapath,
King's College Hospital,
London SE5 9RS
and
Professor of Clinical Biochemistry,
King's College London

BIOGRAPHY

Roy Sherwood is Consultant Clinical Scientist and Scientific Director of Viapath, the pathology laboratories at King's College Hospital. In 2013 he became Professor of Clinical Biochemistry at King's College London. He first became interested in faecal calprotectin as a diagnostic test in patients with gastrointestinal symptoms in the 1990s. The laboratory at King's introduced a routine service for calprotectin in 2000 and currently tests approximately 350 samples a week. In recent years other faecal markers have appeared and were reviewed by Prof Sherwood in the Journal of Clinical Pathology in 2012.

Biomarkers in the Diagnosis and Management of Inflammatory Bowel Disease

Patients attending a gastroenterology out-patients clinic may have inflammatory bowel disease (IBD, ulcerative colitis or Crohn's disease), colorectal cancer or food allergies, but typically 50% have irritable bowel syndrome (IBS). Distinguishing between IBD and IBS is important to reduce the cost and inconvenience to patients of colonoscopy. Similarly, monitoring disease activity in patients with known IBD has benefits in optimising treatment. For diagnosis of IBS the Rome III questionnaire combined with measurement of CRP and ESR is standard practice. In recent years this has been supplemented with the use of faecal markers, especially calprotectin a protein derived from neutrophils.

In the initial study at King's of 620 consecutive GI clinic patients found that a combination of a normal faecal calprotectin, normal intestinal permeability and positive Rome criteria had an odds-ratio of 58 for IBS. Many subsequent studies have found sensitivities and specificities for faecal calprotectin of 90%+ for distinguishing IBS from IBD. There are various Disease Activity Scores (CDAI & UCDAI) for assessing the extent of inflammation but these are based on subjective reporting of symptoms by the patient. Calprotectin has been shown to be superior to these scores in monitoring disease activity and in predicting relapse. It has also been applied to a range of other conditions including small bowel transplantation, graft versus host disease following bone marrow transplants and in acute infectious diarrhoea.

Other faecal markers have been proposed including lactoferrin, S100A12, beta-defensin and M2PK. M2-PK is the dimeric form of pyruvate kinase and was initially proposed as a tumour marker for colorectal cancer with a sensitivity of around 80%. A study at King's, however, found that faecal M2PK was also increased in patients with IBD with active disease due to increased cellular turnover.

Session 3

GENETICS: LABORATORY ASPECTS AND CLINICAL BREAKTHROUGHS

Chair:

Ms. Caroline Joyce

Principal Clinical Biochemist
Cork University Hospital

Dr. Derek Morris

Co-Director, CogGene Group,
National University of Ireland, Galway

**Next Generation Sequencing:
Applications and Challenges in the Clinic**

Dr. Michael Morris

Director, Department of Molecular Diagnostics,
synlab, Lausanne, Switzerland

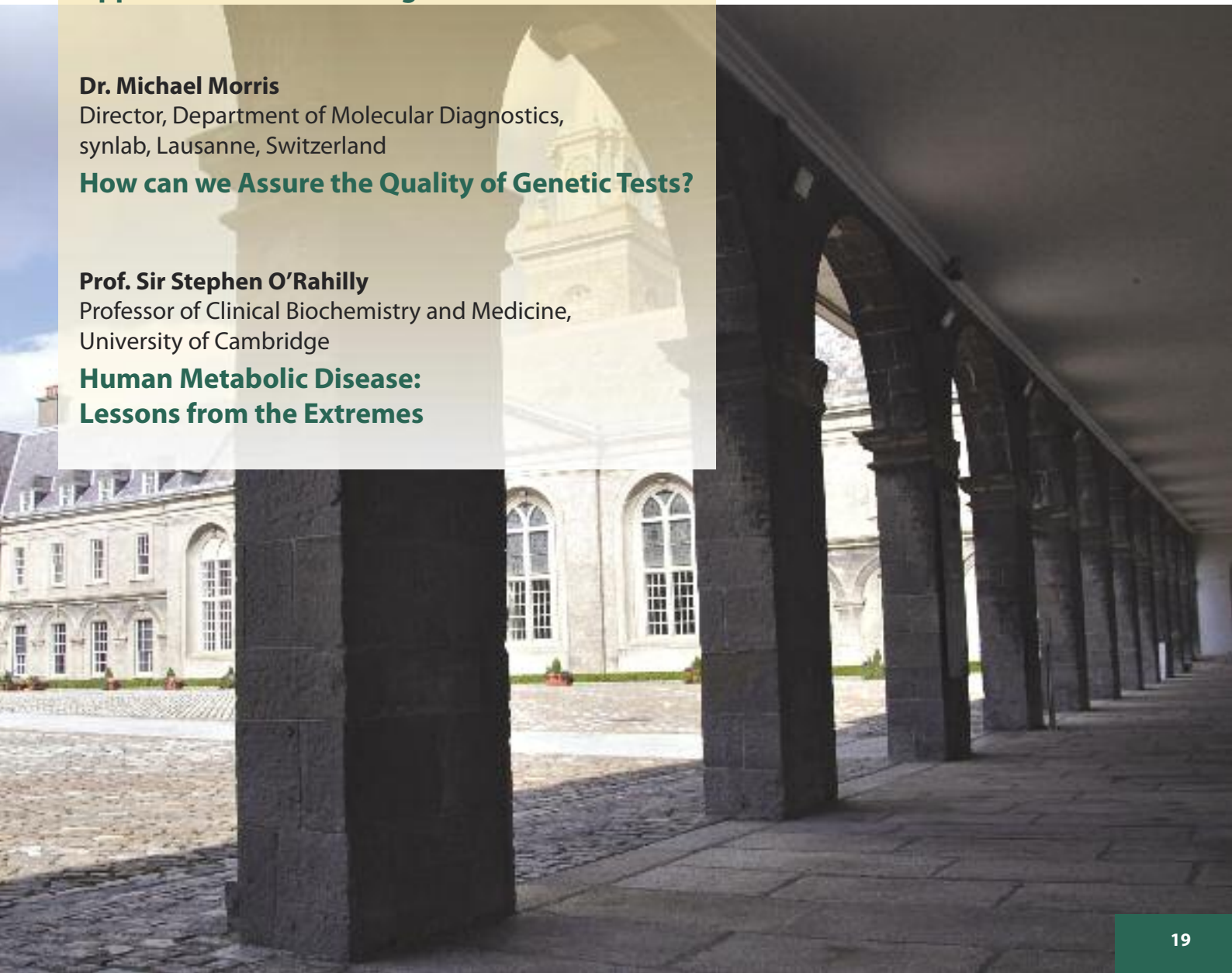
How can we Assure the Quality of Genetic Tests?

Prof. Sir Stephen O'Rahilly

Professor of Clinical Biochemistry and Medicine,
University of Cambridge

**Human Metabolic Disease:
Lessons from the Extremes**

Royal Hospital Kilmainham · through the Arches



Session 3

Dr. Derek Morris
Co-Director CogGene Group,
National University of Ireland,
Galway

BIOGRAPHY

Derek Morris graduated with a B.Sc. in Biotechnology from the National University of Ireland, Galway in 1998. In 2001, he completed his PhD in molecular genetics at the Department of Psychological Medicine, Cardiff University. He subsequently joined the Neuropsychiatric Genetics Research Group in Trinity College Dublin (TCD) as a research fellow and was awarded a HRB Postdoctoral Career Development Research Fellowship in 2003. In 2006, Dr. Morris was appointed Lecturer in Molecular Psychiatry within the Dept. of Psychiatry in TCD and in 2013 moved to NUI Galway where he is now Lecturer in Biomedical Science. Dr. Morris' research interests are the development of novel methods for mapping genes for complex diseases and the application of high-throughput genomics technologies to the detection of risk genes for schizophrenia and bipolar disorder. He has extensive experience of genome-wide association studies and using SFI funding, set up TrinSeq, the first next-generation sequencing lab in Ireland in 2008. He is currently President of the Irish Society of Human Genetics.

Next Generation Sequencing: Applications and Challenges in the Clinic

Next-generation sequencing (NGS) is technology that can generate DNA sequence data in a manner that is cheap, fast and accurate. This talk will provide an introduction to NGS technology and its many applications in molecular biology. The main focus will be applications that involve the use of NGS to assay DNA variation, including methods such as targeted gene sequencing, exome sequencing and whole genome sequencing, and how these techniques can be applied to the study of the genetic basis of human disease. Examples will be provided of how this has achieved massive breakthroughs in the study of both rare and common genetic disorders. The challenge now is to effectively move this technology from the research lab into a clinical setting; what can be achieved and what are the challenges?

Session 3

How Can We Assure the Quality of Genetic Tests?

Quality assurance in genetic testing laboratories has many components, both technical and organisational. Accreditation to ISO 15189 or equivalent is considered as the single most effective route to comprehensive laboratory quality assurance. Validation and verification, closely-related concepts that represent one of the fundamental differences between clinical and research laboratories, are formal requirements of ISO 15189:2012 (section 5.5.1); simplistically, before implementing a new diagnostic test is developed the laboratory must validate it, to show that it is suitable for the intended use and that it achieves the required performance.

Insufficient, useless or inexistent validation is one of the most common deficiencies identified in accreditation audits, and can lead to test failure or incorrect results. The validation of a test is essentially an evaluation of its accuracy, and an understanding of the concepts and parameters of accuracy is an essential prerequisite to performing effective and efficient validation. Accuracy is not measured directly, but through its opposite (measurement uncertainty, or error). As with the vast majority of medical laboratory tests, the raw data of genetic tests is almost invariably quantitative; and for those tests for which a quantitative results is given ("15% mosaicism"), accuracy is simple to address through its components of trueness and precision, with uncertainty being measured as bias and SD respectively. However, genetic tests are unusual in that the results themselves are commonly qualitative ("presence/absence of a variant"). In this situation, it is often more appropriate to determine the qualitative components of accuracy, sensitivity and specificity, with uncertainty being measured with a confidence interval. An international expert group formulated a standardized framework for validation (Mattocks et al 2010) defining different categories of quantitative and qualitative tests and providing a unified approach to planning, performing and documenting test validation. In practice, tests can often be classified in different categories and the choice will be made according to the control samples available.

Dr. Michael Morris
Director, Department of Molecular
Diagnostics, synlab,
Lausanne, Switzerland

BIOGRAPHY

After obtaining his D. Phil. in molecular immunology at Oxford University, Michael Morris moved to Geneva University Hospital in 1988, to establish and direct the molecular genetics diagnostics laboratory. In addition to developing the diagnostic laboratory, Michael has been active in the development of quality assurance in genetics diagnostics. He was the principal author of the Swiss Best Practice Guidelines for Clinical Molecular Genetic Reporting, which are still a reference in Europe, and was a member of the taskforce that developed the Swiss FAMH Specialization in Medical Genetic Analysis. Michael was involved in the gestation, the birth and then the life of EuroGentest, the European Network of Excellence for quality in medical genetics. He is an expert for the European CF Network, a board member of the European Molecular Genetics Quality network (EMQN), and a member of the Swiss Federal Commission of experts for human genetic analysis (GUMEK), as well as author of some 125 scientific publications and guidelines in the field of genetic analysis and quality assurance.

In 2013, Michael took on a new challenge with the synlab laboratory group, where he directs the new Department of Molecular Diagnostics in Lausanne and heads synlab's international genetic advisory board.

Session 3

Professor Sir Stephen O'Rahilly
Professor of Clinical Biochemistry
and Medicine, Head of Department,
Department of Clinical Biochemistry,
University of Cambridge

BIOGRAPHY

Stephen O'Rahilly is Professor of Clinical Biochemistry and Medicine at the University of Cambridge and Honorary Consultant Physician at Addenbrooke's Hospital. He led the establishment of the Institute of Metabolic Science, which he now co-directs. He is Scientific Director of the Cambridge NIHR Biomedical Research Centre. He qualified in Medicine from University College Dublin and undertook post-graduate training in London, Oxford and Boston before setting up his laboratory in Cambridge in 1991. He has sought to better understand the molecular mechanisms leading to diabetes, obesity and related metabolic and endocrine disorders. He remains active in clinical practice and in the teaching of medical students. He has won many national and international awards including the Heinrich Wieland Prize, the Inbev Baillet Latour Prize and the Zülch Prize. He was elected to the Royal Society in 2003, a Foreign Associate of the National Academy of Sciences USA in 2011 and is an Honorary Member of the German Society for Internal Medicine. He was appointed a Knight Bachelor in 2013.

University Degrees

MB BCh BAO 1981 (National University of Ireland)
 MD 1987 (National University of Ireland)

Professional Qualifications

MRCPI (1983); MRCP (UK) (1984); FRCPI (1996);
 FRCP (UK) (1996); FRCPath (2002)

Affiliations

Professor Sir Stephen O'Rahilly, MD FRS FMedSci
 Professor of Clinical Biochemistry and Medicine
 Head of Department, Department of Clinical
 Biochemistry, University of Cambridge
 Director, University of Cambridge Metabolic Research
 Laboratories
 Director, MRC Metabolic Diseases Unit
 Co-Director, Wellcome Trust-MRC Institute of
 Metabolic Science
 Scientific Director, NIHR Cambridge Biomedical
 Research Centre
 Honorary Consultant Physician, Cambridge
 University Hospitals NHS Foundation Trust
 Fellow, Pembroke College, Cambridge
 President, Society for Endocrinology
 Associate Faculty Member, Wellcome Trust Sanger
 Institute, Cambridge

Human Metabolic Disease: Lessons from the Extremes

The genetic component of quantitative metabolic traits is complex with a mixture of common alleles of small effect and rarer alleles of larger effect. We have principally focused on finding the latter through the study of extreme human phenotypes of obesity and insulin resistance, including lipodystrophy. By applying both candidate and hypothesis-free genetic approaches we have identified multiple different genetic variants that cause highly penetrant forms of these diseases. Through detailed phenotypic studies in humans and relevant murine and cellular models, these disorders continue to provide new insights into the physiology and pathophysiology of energy balance and metabolism.

Session 4

CLINICAL CASES/GUEST LECTURE/ POSTER PRIZE

Chair:

Dr. Ned Barrett, Retired Consultant Clinical Biochemist,
University Hospital, Limerick

Ms. Caroline Joyce

Principal Clinical Biochemist, Cork University Hospital

Unravelling a Case of Neonatal Diabetes

Ms. Deirdre Deverell

Principal Clinical Biochemist,
Temple Street Children's University Hospital, Dublin

**Molybdenum Cofactor Deficiency – Diagnostic
Pitfalls on Day 2 of Life**

Dr. Pooler Archbold

Retired Consultant Chemical Pathologist,
Belfast City Hospitals Trust, Northern Ireland

Clinical Biochemistry – a Personal Perspective

**Presentation of Geraldine Roberts Medal
for best scientific poster**

Conference close

Royal Hospital Kilmainham · 'Making notes'



Session 4

Dr. Pooler Archbold
Consultant Chemical Pathologist
(retired).
Belfast City Hospital's Trust,
Northern Ireland

Clinical Biochemistry – a Personal Perspective

A memoir of the changes that have occurred in Clinical Biochemistry across my career and of the people who influenced me during that career.

BIOGRAPHY

Completed a BSc and PhD in Biochemistry before reading Medicine at Queen's University Belfast. Postgraduate training in Chemical Pathology took place in Guildford and Belfast. Became Consultant Chemical Pathologist to Belfast City Hospital in 1989 with clinical interests in endocrinology, diabetes and metabolic bone disease. Retired 2013.



Breakthrough in ovarian reserve indicator reliability

The new AMH Elecsys® test from Roche provides a more reliable indicator of ovarian reserve than manual AMH solutions currently in the market. It produces standardised results whereas those produced by the use of ultrasound (antral follicle count, AFC) often vary depending on the operator or clinic.

The fully automated blood test, which received a CE-mark in July 2014, runs on Roche's highly innovative Electro-Chemiluminescence (ECL) detection technology. It completes and further differentiates Roche's fertility portfolio. It can be performed any time during the menstrual cycle and can be quickly incorporated into routine practice.

The Elecsys® test delivers high precision over the entire measuring range for reliable results and it offers higher

sensitivity for better discrimination of low, normal and high values related to ovarian reserve.

In future, the AMH assay will be used in combination with the new human recombinant FSH treatment, currently in phase III development at Ferring Pharmaceuticals. Roche and Ferring Pharmaceuticals are working towards a companion diagnostic test to be used for individualized fertility management.

The Elecsys® AMH aims to assess anti-Mullerian Hormone levels, a measure of a woman's ovarian reserve, and also of her ovarian response to infertility treatment with gonadotrophin. With this information doctors will be better able to deliver a personalised dose of Ferring's human recombinant FSH based on the woman's AMH level, which uniquely may provide an improved option for couples seeking to conceive through in vitro fertilisation.



Life needs answers

1. Evaluation of novel cardiac biomarkers in the detection of subclinical anthracycline-mediated cardiac side effects

Melissa Jones¹, Dr. Peter O'Gorman², Dr. Maria Fitzgibbon¹

¹Department of Clinical Chemistry and Endocrinology, Mater Misericordiae University Hospital, Dublin,

²Department of Haematology, Mater Misericordiae University Hospital, Dublin

2. Evaluation of biomarkers in renal monitoring of patients treated with anthracycline chemotherapeutic agents

Melissa Jones¹, Dr. Peter O'Gorman², Dr. Maria Fitzgibbon¹

¹Department of Clinical Chemistry and Endocrinology, Mater Misericordiae University Hospital, Dublin,

²Department of Haematology, Mater Misericordiae University Hospital, Dublin

3. The effects of vitamin D supplementation on childhood asthma: a randomized, double-blind, placebo-controlled trial

K. Hutchinson^{1,4}, C. Kerley², B. Elnazir³, D. Couglan³, P. Grealley³, Y. Rochev⁴, J. L. Faul²

¹Biomnis Ireland, Sandyford, Dublin 18, Ireland

²Asthma Research Centre, Connolly Hospital, Dublin 15, Ireland

³Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland

⁴NCBS, National University of Ireland, Galway, Ireland

4. Prevalence of Fentanyl Use in patients using drug addiction services in Ireland

Emma Burke, Sinead McNamara, Louise Lawlor

The National Drug Treatment Centre, Drug Analysis Laboratory

5. Procalcitonin in low risk pregnancy and postpartum period

Shane Deasy, Keelin O'Donoghue, Mary Stapelton, Alice O'Brien, Caroline Joyce

Biochemistry Dept., Cork University Hospital, Wilton, Cork, Ireland

6. Effect of β -adrenoreceptor blocker withdrawal on both plasma renin activity & direct renin concentration

Griffin T¹, Browne G¹, Dennedy MC¹, O'Shea PM²

¹Discipline of Pharmacology & Therapeutics, National University of Ireland, Galway

²Dept of Clinical Biochemistry, Galway University Hospital, Galway

7. Transitioning 'high-sensitivity' troponin into routine diagnostic use. More than just a sensitive issue!

¹Lee GR, ¹Brown T, ²Khan I, ¹Guest B, ¹Fitzgibbon MC

¹Dept. of Clinical Biochemistry and Diagnostic Endocrinology, Mater Misericordiae University Hospital

¹Dept of Cardiology, Mater Misericordiae University Hospital

8. A Study of Androgens and their Clinical Applicability in Polycystic Ovary Syndrome (PCOS) Patients

Sorcha Ni Ghoillidhe, Dr. Maria Fitzgibbon & Dr. Jennifer J Brady

Clinical Chemistry and Endocrinology Department, Mater Misericordiae University Hospital, Eccles St, Dublin 7

9. Low vitamin B12 and elevated folate status in older adults-a risk factor for cognitive impairment?

Eamon Laird¹, Helene McNulty², Mary Ward², Leane Hoey², JJ Strain², Miriam Casey³, Conal Cunningham³ & Anne Molloy¹

¹School of Medicine, Trinity College, Dublin 2 Ireland;

²Northern Ireland Centre for Food and Health, University of Ulster, Coleraine, BT52 1SA, Northern Ireland;

³The Mercers Institute for Research on Ageing, St James's Hospital, Dublin, Ireland

10. Two site comparison of a liquid chromatography mass spectrometry and a competitive binding assay for measurement of 25OH Vitamin D

Liam Blake¹, Paula O'Shea¹, Will McCormack², Catherine Norton², Phil Jakeman²

¹Department of Clinical Biochemistry, Galway Roscommon University Hospitals

²Physical Education and Sport Sciences Department, University of Limerick

11. Establishment of reference intervals for aldosterone & direct renin in an Irish population using the IDS-iSYS automated system

O'Shea PM¹, Brady JJ², Gallagher N³, Fitzgibbon MC²

¹Dept. of Clinical Biochemistry, Galway University Hospital, Galway

²Dept of Clinical Biochemistry & Diagnostic Endocrinology, Mater Misericordiae University Hospital, Dublin

³Dept. of Clinical Biochemistry, Bon Secours Hospital, Galway

12. Validation of the IDS-iSYS newly developed automated direct renin concentration (DRC) assay

O'Shea PM¹, Brady JJ², Gallagher N³, Fitzgibbon MC²

¹Dept. of Clinical Biochemistry, Galway University Hospital, Galway

²Dept of Clinical Biochemistry & Diagnostic Endocrinology, Mater Misericordiae University Hospital, Dublin

³Dept. of Clinical Biochemistry, Bon Secours Hospital, Galway

13. A new era in hypertension diagnostics – Development of a Plasma Metanephrines LC-MS/MS analysis method & establishment of a reference range at the Mater Misericordiae University Hospital

M Rachel Cullen, Keith J Mulready, Jennifer J Brady,

Maria C Fitzgibbon, Marguerite M MacMahon

Department of Clinical Biochemistry & Diagnostic Endocrinology, Mater Misericordiae University Hospital, Dublin 7

14. A new clinical LC-MS/MS method for quantification of the antifungal Voriconazole in Human serum at the Mater Misericordiae University Hospital

Keith J Mulready, Maria C Fitzgibbon, Marguerite M MacMahon

Department of Clinical Biochemistry & Diagnostic Endocrinology, Mater Misericordiae University Hospital, Dublin 7

15. Taking the guesswork out of PCOS – Development of a new LC-MS/MS testosterone & androstenedione method in the Mater Misericordiae University Hospital

Keith J Mulready, Jennifer J Brady, Maria C Fitzgibbon,

Marguerite M MacMahon

Department of Clinical Biochemistry & Diagnostic Endocrinology, Mater Misericordiae University Hospital, Dublin 7

16. Efficacy of body mass index as a predictor of inflammatory disease

B.E. Cronin, P.J. Allsopp, M.B.E. Livingstone, J.M. Wallace and

E.M. McSorley,

Northern Ireland Centre for Food and Health, University of Ulster, Coleraine, BT52 1SA

17. Development of a TPMT test for common and rare genetic variants

T Shannon, VEF Crowley, B MacNamara

Clinical Biochemistry Biochemistry Department, LabMed Directorate, St. James's Hospital, Dublin 8

18. Into the world of genetic validation with *TPMT*

¹Barbara MacNamara, ¹Tom Shannon, ²Jean Dunne,
³Anton Pohanka, ³Larissa Koukel, ¹Vivion Crowley
¹Molecular Diagnostics Laboratory, Dept. Of Biochemistry, St. James's Hospital, Dublin 8.
²Dept. Of Immunology, St. James's Hospital, Dublin 8.
³Dept. Of Clinical Pharmacology, Karolinska Hospital, 14186 Stockholm, Sweden

19. Genetic Test for Ferroportin Disease: From Good to Better

Aoife McConnon, Barbara MacNamara, Alan Balfe, Vivion Crowley
Molecular Diagnostics Laboratory, Dept. Of Biochemistry, St. James's Hospital, Dublin 8

20. Development and validation of mutation scanning assays for Autosomal Dominant Hypercholesterolaemia related to mutations in *LDLR* and *PCSK9*

Sarah Savage, Erum Rasheed, Barbara MacNamara, Vivion EF Crowley
Molecular Diagnostics Laboratory, Biochemistry Department, St James's Hospital, Dublin 8

21. Development and Validation of Mutation scanning assays for the non-acute Erythropoietic Protoporphyrria (EPP) & Familial Porphyria Cutanea Tarda (f-PCT) related to mutations in the *FECH* and *UROD* genes

S Savage, C Lannon, B MacNamara, N Brazil, VEF Crowley
Molecular Diagnostics and Porphyrin Laboratories, Biochemistry Department, St. James's Hospital, Dublin 8

22. A case of Neonatal Diabetes Mellitus responding to Personalised Medicine

Caroline Joyce¹, Mary Stapleton¹, John O'Mullane¹, Frances Ashcroft², Sian Ellard³, Stephen O'Riordan⁴ and Susan O'Connell⁴
¹Department of Clinical Biochemistry Department, Cork University Hospital, Ireland
²Department of Physiology, Anatomy & Genetics, Parks Road, Oxford, UK
³Department of Biomedical & Clinical Science, University of Exeter Medical School, UK
⁴Department of Paediatrics & Child Health, Cork University Hospital, Ireland

23. An Unusual Case of Asymptomatic Jaundice and Isolated Hyperbilirubinaemia

¹A Rakovac Tisdall, ¹V Murphy, ¹S Savage, ¹N Brazil, ²S Norris,
¹VEF Crowley
¹Biochemistry Department, St. James's Hospital, Dublin 8
²Hepatology Centre, St. James's Hospital, Dublin 8

24. From discordant thyroid function tests to unsuspected hypopituitarism: how laboratory liaison can aid diagnosis

Rakovac Tisdall A, Rasheed E, Murphy V, Redha M, Crowley V
Biochemistry Department, St. James's Hospital, Dublin 8

25. Hyper Ig D Syndrome (HIDS): Diagnostic Pitfalls of Urine Organic Acid Analysis

Fitzsimons PE¹, Charleton N¹, Flanagan F³, Moylett E³, Gavin PJ⁴, and Mayne PD^{1,2}.
¹Department of Clinical Biochemistry, Temple Street Children's University Hospital, Dublin.
²Department of Clinical Biochemistry, Our Lady's Children's Hospital, Crumlin, Dublin,
³Department of Paediatrics, University College Hospital, Galway and
⁴Infectious Diseases, Our Lady's Children's Hospital, Crumlin and Temple Street Children's University Hospital, Dublin.

26. Transcription free integration between an ABSciex LC MS-MS API 3200 and the iSOFT Telepath system for routine Vitamin D Analysis

Craig Webster¹, Rachel Henderson, Kevin Jones², Phil Goddard² & Graham Pratt²
¹Birmingham Heartlands Hospital, Bordesley Green East, Birmingham B9 5SS
²CSols Ltd., Runcorn, Cheshire WA7 4QX

27. Improving turnaround times for trace element screening of hip replacement patients using the CSols Links for LIMS system with a Thermo Scientific X Series ICP-MS Mass Spectrometer linked to a Clinisys WinPath LIMS system

Kevin Jones¹ & Graham Pratt¹, Martin Davies² & Chris Harrington²
¹CSols Ltd, Runcorn, Cheshire WA7 4QX, UK
²Supra-Regional Assay Service, Surrey Research Park, Guildford, GU2 7YD, UK

28. Can Harmonised Reference Intervals be Applied in Ireland?

Peadar McGing¹, Bernadette Jackson², Ruth O'Kelly³, Irene Regan⁴, Paula O'Shea⁵, and Hazel Graham⁶.
¹Department of Clinical Chemistry and Diagnostic Endocrinology, Mater Misericordiae University Hospital, Dublin; ACBI,
²Point of Care Manager, Naas General Hospital; AMLS,
³Department of Biochemistry, Coombe Women and Infants University Hospital; ACBI,
⁴Coagulation Department, Our Lady's Children's Hospital, Crumlin, Dublin; AMLS,
⁵Department of Clinical Biochemistry, Galway University Hospitals; ACBI, 6 IEQAS, Unit B06 Nutgrove Enterprise Park, Dublin; IEQAS

29. An E-alert System for Early Detection of Acute Kidney Injury in Hospitalised Patients

Walsh Paul¹, Begley Eoin¹, Boran Gerard¹, Gaffney Peter¹, Lavin Peter², Kennedy Claire²
¹Clinical Chemistry and ²Nephrology Departments, Tallaght Hospital, D24

30. Sensible Test Ordering Practice in an Emergency Department

Gerard Boran, Peter Gaffney, Sarah Condell
Clinical Chemistry Department, Tallaght Hospital, Dublin 24

31. POCT in Action: Addressing Inpatient Glycaemic Control with an Automated Inpatient Glucometry Alert System

Jansen Seheult¹, Agnieszka Pazderska², Peter Gaffney¹, Jane Fogarty¹, James Gibney², Gerard Boran¹
¹Clinical Chemistry Department, Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland
²Department of Medicine - Endocrinology Division, Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland

32. Minimum re-test intervals - An audit of laboratory testing of thyroid function & HbA1c

Dr. Patrick Thompson, Dr. Derek McKillop, Dr. Peter Sharpe
Biochemistry Department, Craigavon Area Hospital, 68 Lurgan Road, Portadown, Co. Armagh

33. Establishment and Validation of a Liquid Chromatography - Tandem Mass Spectrometry Method for the Quantification of Free Urinary Metanephrines

James Kelly, Gerald Cox, Vivion Crowley, Martin Healy
Department of Clinical Biochemistry, Central Pathology, St James's Hospital, Dublin 8

Poster 1

Evaluation of novel cardiac biomarkers in the detection of subclinical anthracycline-mediated cardiac side effects

Melissa Jones¹, Dr. Peter O’Gorman², Dr. Maria Fitzgibbon¹

¹Department of Clinical Chemistry and Endocrinology, Mater Misericordiae University Hospital, Dublin,

²Department of Haematology, Mater Misericordiae University Hospital, Dublin

INTRODUCTION:

Anthracycline chemotherapeutics are successfully utilised in the treatment of solid organ tumours and haematological malignancies. However, their efficacy is compromised by the possibility of cardiac myocyte damage. High sensitive troponin-I (hs-cTnI) and galectin-3 (GAL-3) are novel markers in the detection of cardiac injury.

OBJECTIVE:

To evaluate hs-cTnI and GAL-3 in the detection of anthracycline-mediated subclinical cardiac injury.

METHODS:

Eighty-four patients were recruited (39-anthracycline and 45 non-anthracycline regimes). The anthracycline cohort was divided into 3 groups based on the dosing schedule of the anthracycline (early, continuous and late-dose groups).

A serum sample was collected prior to commencement of chemotherapeutic cycles and analysed for hs-cTnI and GAL-3 using immunoassay (Abbott Diagnostics). Friedman and Wilcoxon tests were employed for statistical analysis.

RESULTS:

The early-dose group demonstrated a rising trend in hs-cTnI ($p < 0.0001$) with median increases from 3.4 ng/L to 32.3 ng/L. A smaller increase from 2ng/L to 4.6 ng/L was observed among the late-dose group ($p < 0.001$). The continuous-dose group demonstrated significant increases in hs-cTnI from 1.9 ng/L to 27.2 ng/L ($p < 0.0001$). No significant changes were observed among the non-anthracycline cohort.

No significant changes in GAL-3 values were observed among patients receiving anthracycline agents after 3 cycles of chemotherapy ($p > 0.05$). GAL-3 values did not vary significantly following 3 months of chemotherapy in patients treated with non-anthracycline agents.

CONCLUSIONS:

The rising trend in hs-cTnI among the anthracycline cohort raises the possibility of subclinical cardiac damage mediated by an anthracycline regimen. Identification of patients at greater risk of cardiac injury may lead to these patients receiving cardio-protective treatment.

No significant changes to GAL-3 were observed, which most likely relates to the early timeframe when it is unlikely that subclinical fibrotic changes would manifest. A long-term evaluation of patients using this marker will yield a more accurate assessment of its clinical utility when related to imaging.

Poster 2

Evaluation of biomarkers in renal monitoring of patients treated with anthracycline chemotherapeutic agents

Melissa Jones¹, Dr. Peter O’Gorman², Dr. Maria Fitzgibbon¹

¹Department of Clinical Chemistry and Endocrinology, Mater Misericordiae University Hospital, Dublin,

²Department of Haematology, Mater Misericordiae University Hospital, Dublin

INTRODUCTION:

Anthracycline chemotherapeutics are efficacious agents, but their clinical utility is limited on account of potential nephrotoxicity. Continuous assessment of renal function is also an important component of chemotherapeutic drug dosing.

Routine biomarkers of renal monitoring such as creatinine are influenced by factors independent of renal function. Neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C are biomarkers which have potential in monitoring renal function.

OBJECTIVE:

To evaluate cystatin C and NGAL in assessing renal function in patients receiving anthracycline chemotherapeutics.

METHODS:

Eighty-four patients were recruited (39-anthracycline and 45 non-anthracycline regimes). A serum and urine sample was collected prior to commencing chemotherapeutic cycles and analysed for cystatin C (immunoturbidometric assay) and NGAL (immunoassay) (Abbott Diagnostics). Mann-Whitney, Spearman and Pearson tests were employed for statistical analysis.

RESULTS:

Median cystatin C concentrations remained relatively stable among the anthracycline cohort. A significant difference in cystatin C was observed between the anthracycline and non-anthracycline cohorts before treatment ($p < 0.01$). Following 5 cycles of treatment and in all subsequent cycles, cystatin C values were significantly lower in patients treated with anthracyclines ($p < 0.01$).

Cystatin C did not correlate to creatinine in the anthracycline cohort ($p > 0.05$) with a better correlation observed among the non-anthracycline cohort ($r = 0.49-0.62$, $p < 0.001$). NGAL values remained consistent among both cohorts ($p > 0.05$).

CONCLUSIONS:

The significant difference in cystatin C after anthracycline therapy may reflect anti-tumour activity and decreasing tumour burden. This activity may explain the paucity of a correlation between cystatin C and creatinine in assessing renal function. NGAL did not provide additional value in this setting.

There is much debate as to the optimal biomarker of kidney dysfunction, particularly, in patients with malignancy. Both cystatin C and creatinine may have advantages and disadvantages in this cohort. Further investigations will elucidate their role in estimating glomerular filtration rate, used for drug dosing in an oncology setting.

Poster 3

The effects of vitamin D supplementation on childhood asthma: a randomized, double-blind, placebo-controlled trial

K. Hutchinson^{1,4}, C. Kerley², B. Elnazir³, D. Coughlan³, P. Greally³, Y. Rochev⁴, J. L. Faul².

¹Biomnis Ireland, Sandyford, Dublin 18, Ireland.

²Asthma Research Centre, Connolly Hospital, Dublin 15, Ireland.

³Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland.

⁴NCBES, National University of Ireland, Galway, Ireland.

Vitamin D deficiency (VDD) and asthma-incidence/severity share many common risk factors. Vitamin D has a number of biological effects that are likely important in regulating key mechanisms in asthma, including immunomodulatory effects as well as altering airway hyperresponsiveness, pulmonary function, airway smooth muscle-remodeling and response to anti-asthma therapy. Thus, VDD may result in increased prevalence and severity of childhood asthma.

In Winter 2013-2014 we recruited 43 children (23 male), aged 5-15 (mean 8.7y) with a mean body mass index (BMI) of 19.9 kg/m² (13 - 32.6) all previously diagnosed with asthma. At baseline and after 15 weeks of daily supplementation with 2,000 IU vitamin D3 or matching placebo, we assessed: pulmonary function, asthma control, quality of life. Vitamin D (25(OH) D), calcium, PTH, phosphate, IgE and hsCRP were measured using an Abbott Architect ci8200.

At baseline: mean 25(OH) D was 51nmol/L (24-80). According to the *Institute of Medicine* guidelines, 21 children had deficient levels (<50nmol/L), while 22 had sufficient 25(OH)D levels (>50nmol/L). There was no significant difference in demographics, serum markers or self-reported measures of asthma control between the two groups. However, pulmonary function was significantly higher in the vitamin D sufficient group, including forced vital capacity FVC% (66 vs. 96%; p = 0.03) and forced expiratory volume FEV1% (93 vs. 102%; p = 0.03). Negative correlation was found between IgE and Vitamin D levels (p=0.03).

After the supplementation, compliance was high in both groups (>85%). There were no adverse effects. Despite a significant increase in serum 25(OH) D, there was no significant difference between vitamin D supplements and placebo in terms of pulmonary function, subjective asthma measures and serum biomarkers.

Our results agree with a recent, randomized controlled trial of vitamin D replenishment in paediatric asthma. ¹Vitamin D supplementation warrants further investigation in asthmatic children.

¹*Paediatric Pulmonology 2014 doi: 10.1002/ppul.23076.*

Poster 4

Prevalence of Fentanyl Use in patients using drug addiction services in Ireland

Authors: Emma Burke, Sinead McNamara, Louise Lawlor,
The National Drug Treatment Centre, Drug Analysis Laboratory.

Fentanyl is a narcotic opioid analgesic and is around eighty times more potent than morphine. It has been found on the illicit drug market and is sometimes used as a replacement to heroin with its street names reflecting this, for example 'China white', 'white heroin', or simply 'heroin'. Drug users are often unaware they are consuming fentanyl, and due to the high level of potency fatal overdoses have occurred. In Europe growing trends of fentanyl use appear to be emerging with heroin shortages.

Levels of fentanyl abuse have been low in Europe, but even with low levels of abuse, it merits monitoring as it is a 'high risk/harm substance'. EMCDDA 2012 research advises that the European market is becoming less attracted to heroin, than it has been ever before and heroin shortages are being directly linked to abuse of other synthetic opioids (fentanyl, buprenorphine, and methadone).

As little is known on the prevalence of fentanyl use in Ireland, a study was conducted to detect the extent of use/abuse in a cohort of patients attending addiction clinics across Ireland.

The DRI® Fentanyl Assay immunoassay was selected as the screening analysis for the detection of fentanyl in urine. This was performed on a Beckman Coulter AU2700® chemical analyser, positive results were confirmed using LCMS.

A total of 741 samples were analysed, using a regional cross section of urine samples across Ireland. In total, three samples screened positive for Fentanyl. Of the 3 samples tested, none of the clients were known to be prescribed Fentanyl. The data therefore illustrates that fentanyl, although not greatly prevalent in this cohort of patients, is being used in Ireland.

Poster 5

Procalcitonin in low risk pregnancy and postpartum period

Shane Deasy, Keelin O'Donoghue, Mary Stapelton, Alice O'Brien, Caroline Joyce.

Biochemistry Dept., Cork University Hospital, Wilton, Cork, Ireland.

BACKGROUND:

Maternal sepsis can affect all healthy pregnancies. The risk in an immunocompromised pregnant population increases when opportunistic pathogens are introduced into the body before and after delivery (e.g. during standard vaginal, instrumental and caesarean section deliveries). The incorporation of the electro-chemiluminescent Elecsys BRAHMS Procalcitonin (PCT) assay into the Biochemistry Department in Cork University Hospital aims to flag sepsis in healthy pregnant women earlier and with a higher diagnostic accuracy than the current biochemical marker used; C- Reactive Protein (CRP). The development of a PCT reference range in healthy pregnancy may aid in diagnosis, prognosis and treatment protocols in cases of maternal sepsis.

METHOD:

A population of 102 consented to this pilot study. The population consisted of a healthy control group during third trimester pregnancy, a day 1 pre-delivery test group and a day 3 post-delivery test group. The test groups were further divided into mode of delivery; Standard Vaginal Delivery, Instrumental, Elective Caesarean and Emergency Caesarean. Preliminary pregnancy specific ranges were established for PCT and CRP using the Tukey statistical method. PCT and CRP correlation and comparison studies were performed to examine their relationship during (Day 0), before (Day 1) and after (Day 3) pregnancy and the impact delivery methods have on PCT and CRP concentrations was established.

RESULTS:

PCT and CRP reference ranges during third trimester pregnancy were established and ranged between 0.362-0.432 ng/ml and 4.33-6.66 ng/ml respectively. Serum PCT levels were found to increase in the pre-delivery and post-delivery test groups but CRP demonstrated a higher rate of non-specific elevation when compared to healthy controls ($p < 0.01$). Birthing method was demonstrated to impact on both PCT and CRP concentration when compared to healthy controls ($p < 0.01$). Both PCT and CRP concentrations were observed to be elevated during elective and emergency pre-delivery and post-delivery states.

CONCLUSION:

This study supports the future introduction of the Elecsys Brahms PCT assay into the Biochemistry Department in Cork University Hospital as a biomarker for detecting bacterial infection and sepsis during and after pregnancy.

Keywords: Procalcitonin, C-Reactive Protein, postpartum, Reference Range, Sepsis.

Poster 6

Effect of β -adrenoreceptor blocker withdrawal on both plasma renin activity & direct renin concentration

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BACKGROUND:

Primary hyperaldosteronism (PHA) is a common cause of hypertension and is underdiagnosed due to difficulty in interpreting the main screening test, specifically the aldosterone renin ratio (ARR).

β -blockers may produce false positive results due to renin suppression. We investigated the effect of β -adrenoreceptor blocker withdrawal in a cohort of individuals on long-term β -blocker therapy for blood pressure (BP) control.

METHODS:

Poorly controlled hypertensives were recruited and followed-up for 8 weeks. β -blockers were withdrawn at the first clinic visit. At this and each follow-up visit, subjects had BP measured and blood drawn for measurement of renin, aldosterone and routine biochemistry. BP was optimised by maximising non-renin suppressing antihypertensive agents.

AIM:

The objective of this study was to evaluate renin recovery (plasma renin activity (PRA) and direct renin concentration (DRC)) post β -blocker withdrawal.

RESULTS:

Twenty two patients were enrolled under informed consent. β -blocker withdrawal produced a rapid recovery of both PRA and DRC within 2 weeks, with >50% recovery seen at this time point. BP and medication compliance improved in all patients. Interpretation of ARR on β -blockade produced false positive results in 40% of subjects. PRA values (Range: <0.2 to >25ng.mL.h) and DRC results (Range: 4.9 to >550 μ U/mL) were in accord and consistent with clinical assessment. Spearman correlation = 0.868 (CI 0.788 – 0.919; P= <0.001).

CONCLUSIONS:

Screening for PHA using the ARR with patients off all potentially interfering medications is seldom possible. Opinions are divided on whether β -blockers significantly affect the ARR. This study demonstrates a high false positive rate for PHA in those patients taking β -blockers. Notably, β -blocker withdrawal was well tolerated, BP control easily optimised and the accuracy and clinical utility of the ARR improved within 2 weeks of medication withdrawal. This study provides convincing data to support β -blocker withdrawal two weeks in advance of ARR screening for PHA.

Poster 7

Transitioning 'high-sensitivity' troponin into routine diagnostic use. More than just a sensitive issue!

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INTRODUCTION:

High sensitivity cardiac troponin T and I (hs-cTnT and hs-cTnI) assays show better performance than less sensitive contemporary (cTn) assays for the biochemical diagnosis of AMI. We report on our approach to implementing an hs-cTnI assay for this purpose.

METHODS:

Analytical imprecision and inaccuracy for the hs-cTnI assay (Abbott laboratories) were verified as per standard laboratory procedures. Over a one month period (March 2013) paired cTnI and hs-cTnI measurements were obtained for 1119 patients. Result concordance was determined by evaluating data against unisex (cTnI: 30 ng/L, hs-cTnI: 25 ng/L) and gender-specific 99th centiles (hs-cTnI: M: 34/F: 16 ng/L), used for diagnosis. Discordant data was correlated to available clinical and laboratory information and following cardiology evaluation, patients were adjudicated to a diagnosis of either Acute Coronary Syndrome (ACS) or Non-ACS.

RESULTS:

The hs-cTnI showed acceptable imprecision and inaccuracy across the analytical range, including concentrations <99th centile. Both assays were highly concordant (94.5%) with discordant results (4.5%, n=60) characterised mainly by patients (n=43/60) with elevated hs-cTnI but not cTnI. Discordance between assays was higher (8.3%, n=91) when gender-specific cut-offs were used for evaluating hs-cTnI data, attributable mostly to female patients, as expected. 12 patients in the discordant sub-cohort were adjudicated to a diagnosis of ACS, including 6 patients (2M, 4F) with cTnI values <99th centile (FNs). 2 female ACS patients had hs-cTnI results <99th centile (FNs) but not the >female 99th centile (TPs) whereas 6 male ACS patients had hs-cTnI results <male 99th centile (FNs) but not the (lower) unisex cut-off value.

CONCLUSION:

From a sub-cohort of patients showing discordant cTnI and hs-cTnI results we have confirmed reports of improved sensitivity using gender-specific reference ranges. Our findings have informed design of a diagnostic algorithm supporting the appropriate use and interpretation of hs-cTnI measurements in the biochemical investigation of AMI.

Poster 8

A Study of Androgens and their Clinical Applicability in Polycystic Ovary Syndrome (PCOS) Patients

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OBJECTIVE:

To investigate androgen (testosterone, androstenedione and DHEAS) secretion patterns in Polycystic Ovary Syndrome (PCOS) patients and how they contribute to the diagnosis of PCOS using the Rotterdam criteria.

STUDY DESIGN:

A cohort (n=23) of patients with suspected or confirmed PCOS was recruited from local Endocrine Clinics. Testosterone, androstenedione and DHEAS were measured by LC-MS/MS. We investigated how many of the Rotterdam criteria each of the patients displayed by analysing the laboratory results and from the information retrieved from the charts, including menstrual history, hirsutism, radiology reports, age, exclusion of other conditions, and medication.

RESULTS:

Out of the 23 PCOS patients, 15 had both testosterone and androstenedione measured. There were no patients with testosterone only raised, 3 (20%) patients had testosterone and androstenedione raised, 4 (27%) patients had androstenedione only raised and 8 (53%) patients had neither testosterone nor androstenedione raised.

There were 8 patients with measurements of testosterone, androstenedione and DHEAS. Two patients (25%) had a raised DHEAS (1.3-8.5nmol/L) measurement, with one (12.5%) of these having DHEAS as the sole raised measurement.

Eighteen patients had data on all three of the Rotterdam criteria; oligoovulation and/or anovulation (menstrual disturbance), excess androgen activity, polycystic ovaries (by gynaecologic ultrasound). There were no patients with clinical or biochemical hyperandrogenism only, nor with ultrasound evidence of polycystic ovaries only. There were 5 patients with hyperandrogenism and menstrual disturbances, two patients with menstrual disturbances only, five patients with menstrual disturbance and PCOS upon ultrasound and six patients who displayed all three criteria. Sixteen patients out of 18 were therefore diagnosed with PCOS.

CONCLUSION:

This study emphasises the importance of androstenedione and DHEAS measurement as well as testosterone in the diagnosis of biochemical hyperandrogenism in PCOS in the context of the Rotterdam criteria.

Poster 9

Low vitamin B12 and elevated folate status in older adults-a risk factor for cognitive impairment?

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BACKGROUND:

Studies post mandatory folic acid fortification in the US suggest that older adults with high folate but low vitamin B12 status have higher methylmalonic acid (MMA) and homocysteine (tHcy) concentrations as well as a higher risk of cognitive impairment compared to those with low B12 and normal folate status¹⁻⁴. However, studies from countries with voluntary but not mandatory folic acid fortification do not support these findings^{5,6}. Therefore, the aim of the study was to investigate the effect of folate status on markers of B-12 deficiency in relation to cognitive function and frailty in a large, well-characterized older adult population.

METHODS:

Participants (n 5186) were from the Trinity Ulster Department of Agriculture (TUDA) Study, a large study of older Irish adults designed to investigate gene-nutrient interactions in the development of chronic diseases of ageing. Participants were recruited from General Practitioner practices in the Western and Northern Health and Social Care Trusts, Northern Ireland and those attending the memory and bone clinics in the Geriatric Unit of St. James Hospital, Dublin, Ireland. Blood samples were analysed for total serum cobalamin, holotranscobalamin, homocysteine (tHcy), red blood cell (RBC) folate and serum folate. Methylmalonic acid (MMA) determination was performed on a subset of samples (n 1399). Hematologic and renal function data were available through the main study database. Cognitive function was assessed by repeatable battery for the assessment of neuropsychological status (RBANS) with a score <80 indicating cognitive impairment. The population was divided into 4 categories based on serum B12 (<148 compared to ≥148 pmol/L) and serum folate (< 60 and ≥ 60 nmol/L) concentrations.

RESULTS:

There were no significant differences in the concentration of total cobalamin, holo-TC, MMA, tHcy, creatinine, GFR or prevalence of cognitive impairment between participants with either low B12:normal folate (profile 1) or low B12:high folate status (profile 2). However, there were a larger number of subjects in profile 2 with anemia (44% vs 27%; P=0.009) and frailty (62% vs. 43%; P=0.013) compared with profile 1. These differences were no longer significant when examined in the oldest group of participants (>80 yrs).

CONCLUSION:

In this older adult cohort, there was no conclusive evidence of exacerbation of indicators of B12 deficiency in those with elevated folate status. These results could indicate that the selection criteria of B12/folate groups predominately selects the oldest old, (who are the frailest and most heavily supplemented with folic acid) into the low B12 elevated folate group which could give the perception that high folate is the cause rather than a bystander of worse indicators of B12 deficiency.

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Poster 10

Two site comparison of a liquid chromatography mass spectrometry and a competitive binding assay for measurement of 25OH Vitamin D

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Our two laboratories compared the results of 25OH Vitamin D measurements on serum samples using two analytical methods. Our objective was to compare these two methods in routine settings.

Liquid chromatography/mass spectrometry (LC/MS) is used as the method of measuring 25OH Vitamin D in the hospital setting. The MassChrom 25-OH-Vitamin D3/D2 kit (Chromsystems Munich) is used with an Agilent 1290 UPLC and 6440 Triple Quad LC/MS to measure 25 OH Vitamin D3 and 25 OH Vitamin D2 in patients serum samples. The sum of these parameters is reported as 25 OH Vitamin D. On-line solid phase extraction after protein precipitation is employed.

The Elecsys Vitamin D Total (Roche Diagnostics, Mannheim Germany) for measurement of 25 OH Vitamin D is used in the research laboratory. This assay employs a competitive test principle using recombinant Vitamin D Binding Protein (VDBP) as a capture protein to bind 25OH Vitamin D3 and 25OH Vitamin D2.

98 patient, and 97 study participant, serum samples were assayed at both sites. For all samples (n=195) the correlation coefficient was 0.94 between the assays. Passing Bablock regression analysis yielded a slope of 1.045; 95% confidence interval (CI) 1.00 – 1.03; intercept, 6.2 nmol/L (95% CI 9.38 3.00). For samples with 25 OH Vitamin D2 and 25 OH Vitamin D3 detected (n=32) by the LC/MS method, the correlation coefficient was 0.92 between the assays. Passing Bablock regression analysis yielded a slope of 0.964 (95% CI 0.750 – 1.180); intercept, 7.5 nmol/L (95% CI 18.1 3.3). For samples with only 25 OH Vitamin D3 detected by the LC/MS method (n=163), the correlation coefficient was 0.94 between the assays. Passing Bablock regression analysis yielded a slope of 1.043 (95% CI 1.000 – 1.103); intercept, 5.3 (95% CI 8.7 3.0).

When compared across two sites, the Roche Elecsys Vitamin D Total assay correlates well with the MassChrom 25-OH-Vitamin D3/D2 kit on the Agilent platform.

Poster 11

Establishment of reference intervals for aldosterone & direct renin in an Irish population using the IDS-iSYS automated system

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BACKGROUND:

Measurement of aldosterone and or renin is essential to aid the differential diagnosis of secondary hypertension, guide strategy for the therapeutic management of hypertension, and assess adequacy of mineralocorticoid replacement in Addison's disease and congenital adrenal hyperplasia.

AIM:

The objective of this study was to establish normative data for aldosterone and direct renin using newly developed immunochemiluminometric assays on the IDS-iSYS automated platform in an Irish population.

METHODS:

The authors' recruited 207 healthy Caucasian subjects aged 20-65 years (females: n=145). Subjects were ambulatory and attended clinic for blood pressure (BP) measurement and phlebotomy between the hours of 7-11am. BP was measured according to the 2013 European Society of Hypertension/ Cardiology guidelines, clinical information (age, gender, ethnicity, current medications, Body Mass Index, pregnancy status) recorded. All subjects had normal electrolytes and renal function. Blood for aldosterone and direct renin was collected into ethylene diamine tetraacetic acid (EDTA) specimen tubes. Samples were kept @ room temperature and transported within 30 minutes of blood draw to the laboratory for immediate processing (centrifugation, separation and freezing of plasma). Plasma was stored @ -20°C prior to analysis on the IDS iSYS instrument. Data was analysed using Minitab Release version 16. Outliers were removed using the Dixon/Reed one-third rule. Nonparametric analysis of the data was performed, followed by the establishment of the 2.5th and the 97.5th reference limits.

RESULTS:

The reference population had a median age of 41years (Range: 20-65years), normal BP (mean Systolic: 121mmHg (range 96-139mmHg), mean Diastolic: 74mmHg (range 57-89mmHg). The established reference intervals in an Irish Caucasian population for aldosterone and direct renin were 138-1179 pmol/L and 6.5-71.0µIU/mL respectively.

CONCLUSION:

The reference intervals for aldosterone and direct renin using the IDS iSYS assays will permit rapid stratification of patients with refractory hypertension and optimization of therapeutic management of patients.

Poster 12

Validation of the IDS-iSYS newly developed automated direct renin concentration (DRC) assay

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BACKGROUND:

Renin is a proteolytic enzyme synthesised and released by juxtaglomerular cells in response to low blood pressure or low sodium. Measurement of renin is essential in the evaluation of patients with suspected primary hyperaldosteronism (PHA).

AIM:

To assess the performance characteristics and clinical utility of the IDS-iSYS direct renin concentration (DRC) assay.

METHODS:

Renin was measured using the IDS-iSYS DRC assay. This immunochemiluminometric assay employs two different monoclonal antibodies against renin and is calibrated to the WHO IS 68/356. Ethylene diamine tetraacetic acid (EDTA) plasma from patients with selected diagnoses and from healthy Caucasian normotensive subjects was used to assess the potential of DRC alone as a screen for PHA.

RESULTS:

The between-run analytical coefficient of variation (CVA%) at a mean renin concentration of 14 μ UI/mL, 100 μ UI/mL and 390 μ UI/mL was 7.7%, 8.4% and 4.9% respectively. The limit of quantitation = 4.8 μ UI/mL. The mean absolute bias determined using proficiency testing samples (n=15) was 0.545 μ UI/mL (C.I. -0.735–1.83) or 2.37%. Stability of DRC in EDTA whole blood @ RT was 96hrs and @ 4°C was 24hrs. Repeated freezing and thawing of plasma samples had a significant impact on the measurement of DRC and is not recommended. Assay throughput = 76 tests per hour and cost per reportable test ~€9.17 excluding VAT. A total of 337 subjects, controls (n=226), PHA (n=12), and essential hypertension (n=99) were used to determine the decision threshold for case detection of PHA. ROC curve analysis gave the area under the curve (AUC) = 0.946 (CI 0.917 to 0.968:), P = <0.001 for a DRC \leq 14.2 μ UI/mL with diagnostic sensitivity and specificity of 100% and 78.2% respectively.

CONCLUSION:

The performance characteristics of the new IDS-iSYS direct renin concentration assay demonstrate its potential value in case detection of PHA and will offer more timely and effective patient management.

Poster 13

A new era in hypertension diagnostics – Development of a Plasma Metanephrines LC-MS/MS analysis method & establishment of a reference range at the Mater Misericordiae University Hospital

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OBJECTIVE:

Pheochromocytoma is a rare, catecholamine-producing tumour and its presence must be considered in many patients presenting with hypertension. HPLC methods with electrochemical detection have been used to detect metanephrine (MN), normetanephrine (NMN) and 3-methoxytyramine (3MT) but are labour-intensive & time consuming while immunoassay methods can suffer from cross-reactivity & non-specific binding. We describe a highly specific & sensitive Mass Spectrometry (LC-MS/MS) method and establishment of a reference interval for plasma metanephrines. This system has the capacity to analyse large numbers of samples suitable for use in a routine clinical setting.

STUDY DESIGN:

Calibrator/QC/Plasma were prepared using an automated reverse phase/ion-exchange extraction procedure and analyzed by LC-MS/MS HILIC chromatography using an Acquity UPLC linked to a Xevo TQ. Water loss transitions were detected in positive electrospray ionization mode using multiple reaction monitoring. EDTA blood samples, held on ice, were separated & frozen within 1 hr of phlebotomy.

RESULTS:

Functional sensitivity for MN, NMN & 3-MT were found to be 40, 60, & 65 pmol/L respectively. The assay was linear ($r^2 > 0.999$) up to 18050, 18982, 20156 pmol/L with an absence of carryover. Inter- and intra assay precision was <7% for all three analytes. To ensure interference was minimised, quantifier & qualifier transitions for 3MT (m/z 151.1-119.1 and m/z 151.1-91.1) were monitored. The total analysis time per sample was 5.5 minutes. The reference intervals for MN, NMN were determined as 61-377 and 182-867 pmol/L respectively.

CONCLUSION:

We are the first clinical laboratory in Ireland to have developed a robust, high throughput and rapid LC-MS/MS method for the quantitation of plasma free metanephrines. Analysis of 3MT, a potential novel biomarker for metastatic pheochromocytoma & paraganglioma, is a component of the method. This cost-effective method benefits from increased specificity and accuracy compared with immunoassay methods.

Poster 14

A new clinical LC-MS/MS method for quantification of the antifungal Voriconazole in human serum at the Mater Misericordiae University Hospital

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OBJECTIVE:

Voriconazole is a triazole antifungal medication used to treat serious & invasive fungal infections generally seen in patients who are immunocompromised. Voriconazole oral bioavailability is estimated to be 96% with < 2% of the dose excreted unchanged in the urine. It has a variable half-life ($t_{1/2}$) depending on many factors: age (children metabolise the drug more rapidly), hepatic dysfunction, and drug-drug interactions (e.g. sirolimus, rifampin). Correlation between low serum concentrations & therapeutic failure, high concentrations & hepatic toxicity combined with large inter- & intra-patient variability emphasises the importance of therapeutic drug monitoring, particularly in patients with symptoms of toxicity or therapeutic failure. Our aim was to develop & validate an assay for voriconazole using the gold standard method of mass spectrometry (LC-MS/MS) for routine clinical use according to FDA guidelines for Bioanalytical Method Validation.

STUDY DESIGN:

Serum samples were prepared using an automated precipitation/dilution procedure & analyzed by LC-MS/MS using positive electrospray ionization with multiple reaction monitoring following separation by reverse phase chromatography on a C18 UPLC column. Turnaround times (TAT) & requesting patterns following introduction of the LC-MS/MS assay were investigated.

RESULTS:

The assay was linear ($r^2 > 0.997$) up to 13 mg/L with an absence of carryover. Inter- and intra assay precision was <5.4% and functional sensitivity for Voriconazole was found to be 0.10 mg/L. To ensure absence of potential interference, quantifier & qualifier transitions for voriconazole were monitored. There was excellent concordance with sample from the UKNEQAS antifungal scheme. The total analysis time per sample was 3 minutes. The therapeutic range used was 1.3-5.7 mg/L. Voriconazole assay repatriation has significantly reduced TAT from 14 to 2 days. There has also been an overall increase in samples received of 30%. Of note, there was a 7-fold increase in requests received from the MMUH Infectious Disease service since the assay was introduced.

CONCLUSION:

We have developed a robust, high throughput and rapid LC-MS/MS method for the quantitation of serum voriconazole, the first in a clinical laboratory in Ireland. This cost-effective method benefits from increased specificity and accuracy and reduced assay TAT. The MMUH is currently the only clinical laboratory providing this LC-MS/MS assay & has the capacity to be a referral site for this esoteric test.

Poster 15

Taking the guesswork out of PCOS – Development of a new LC-MS/MS testosterone & androstenedione method in the Mater Misericordiae University Hospital

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OBJECTIVE:

Serum testosterone concentrations can assist in the diagnosis of polycystic ovarian syndrome (PCOS), hypogonadism, precocious or delayed puberty, androgen deficiency in men and certain cancers. Androstenedione, a precursor of testosterone, is also produced by the ovaries & adrenals can also be generated in peripheral tissues. It is suggested that approximately 10% of PCOS can be misclassified if androstenedione is not measured. Interference with structurally related steroids is found in commonly used immunoassay methods. Tandem mass spectrometry (LC-MS/MS) provides an accurate & precise methodology to ensure more definitive diagnosis, simultaneously measuring both of these steroids. This will be particularly useful in assessment of females presenting with the clinical features of hyperandrogenism.

STUDY DESIGN:

Calibrator/QC/serum samples were prepared using an automated reverse phase/ion-exchange extraction procedure and analysed by LC-MS/MS using an Acquity UPLC chromatography system linked to a Xevo TQ. Quantifier & qualifier transitions were detected in positive electrospray ionization mode using multiple reaction monitoring. The method also chromatographically resolved epi-testosterone from testosterone.

RESULTS:

Average intra- and inter-assay precision were for testosterone (male & female) <4.0% & <7.2%, for androstenedione <4.4% & 7% respectively. Functional sensitivity for testosterone & androstenedione were found to be 0.14 & 0.13 nmol/L respectively. The assays were both linear ($r^2 > 0.997$) up to 67 nmol/L with an absence of carryover. The total analysis time per sample was 3.8 minutes. The testosterone assay is metrologically traceable to the primary standard M914. Excellent concordance was found with method mean values for testosterone (M & F) and for androstenedione with UKNEQAS samples. The reference interval was determined as <1.8 nmol/L for female testosterone.

CONCLUSION:

This is the first combined testosterone & androstenedione LC-MS/MS method in a clinical laboratory in Ireland. It is robust, rapid & has a high throughput. This cost-effective method benefits from increased specificity and accuracy compared with immunoassay methods.

Poster 16

Efficacy of body mass index as a predictor of inflammatory disease

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The quantity and distribution of body fat are recognised as key risk factors for the development of inflammatory related diseases⁽¹⁾. A direct association between the expression of inflammatory markers such as C-reactive protein (CRP) and body mass index (BMI) has been demonstrated. However, BMI is limited in that it is unable to distinguish between the two components of body mass: fat mass (FM) and fat free mass (FFM)⁽²⁾, both of which are fundamental in identifying inflammatory disease risk. Recently, more direct measures of body composition such as dual-energy X-ray absorptiometry (DXA) have been used, yet uncertainty remains as to which method is most effective in predicting inflammatory disease risk⁽³⁾. The aim of this study was to examine the efficacy of both BMI and DXA as predictors of inflammatory disease risk.

A total of 140 young adults (mean BMI 24.8 (SD 3.6) kg/m²) aged 19-55 years participated in an observational study. BMI, waist circumference, FM (kg), FFM (kg), trunk fat (%) and lean mass (kg) (determined by DXA) were measured and a fasting blood sample was obtained to measure CRP concentrations. Statistical significance was set at $P < 0.05$. Moderate significant correlations were observed between CRP and body composition; BMI ($r = 0.27$), waist circumference ($r = 0.22$), FM ($r = 0.31$) and trunk fat ($r = 0.35$). Of interest, a significant correlation was seen between FM and CRP but there was no significant correlation between FFM and lean mass, supporting the role of adipose tissue as a source of inflammatory biomarkers.

Although CRP is a good indicator of acute inflammation it may not be the best predictive marker of chronic inflammation. In conclusion, our findings demonstrate that BMI is as effective a measure of body composition as DXA in predicting inflammatory disease risk but further analysis of additional biomarkers is warranted.

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Poster 17

Development of a TPMT test for common and rare genetic variants

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INTRODUCTION:

Thiopurine methyltransferase (TPMT) is a phase II cytosolic drug metabolising enzyme that catalyses the methylation of thiopurine drugs such as 6-mercaptopurine and azathiopurine used in the treatment of acute lymphoblastic leukaemia and inflammatory bowel disease. TPMT activity is inherited as a monogenic co-dominant trait. TPMT genetic variants TPMT*2, TPMT*3A, TPMT*3B and TPMT*3C are known to have a negative impact on TPMT enzyme activity. The TPMT gene variants are established pharmacogenetic markers as individuals with a heterozygous or homozygous variant may have an increased risk of adverse thiopurine drug toxicity due to lower TPMT enzyme activity. A TPMT genotyping service is not currently available in Ireland.

AIM:

To develop a mutation scanning assay for TPMT to screen for common and rare genetic variants. This can potentially lead to improved care of patients undergoing thiopurine therapy by pharmacogenetic dosing.

MATERIAL AND METHODS:

A mutation scanning assay incorporating end-point PCR and direct nucleotide Sanger deoxynucleotide sequencing was developed. Using the NCBI TPMT reference gene (NG_012137.1) (<http://www.ncbi.nlm.nih.gov/nucleotide/>) and Primer 3 Blast software, 8 PCR/sequencing primer sets were designed for exons 2 to 9 according to Eurogentest best practice guidelines. Human molecular diagnostic anonymised DNA controls were used for optimisation and primer specificity studies. PCR conditions of each primer set were optimised for annealing temperature, annealing time, elongation time and MgCL2 concentration.

Sanger sequencing was performed and quality of raw sequencing data was examined by creating DNA chromatograms by Seqman-Pro module, while primer specificity was confirmed by aligning test sequences to the reference gene using the MegAlign module of (Lasergene® v11.0).

RESULTS:

Eight PCR/Sequencing primer sets were successfully developed and optimised for each exon. Primers designed were 100% specific for intended target with full coverage of exonic DNA. Three sequencing primers need further design consideration due to the interference of intronic homopolymers on the resolution of the sequencing read.

CONCLUSION:

The assay developed herein has the potential to detect both common and novel variants in exons 2 - 9 of the TPMT gene. Analytical validation is on going. A TPMT genotyping assay coupled with TPMT phenotyping could potentially be used in the clinical assessment and decision of thiopurine treatment in individual patient cases.

Poster 18

Into the world of genetic validation with TPMT

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INTRODUCTION:

Accurate assessment of a patient's Thiopurine methyltransferase (TPMT) status prior to thiopurine therapy can be best achieved by a coupled genotyping-phenotyping approach. The detection of heterozygote or homozygous SNPs in the TPMT gene is mirrored by a decrease or absence of TPMT enzymatic activity and indicates the increased risk of adverse thiopurine drug toxicity. A TPMT genetic screening test should identify TPMT*1 wildtype, TPMT*2, TPMT*3A and TPMT*3B genotypes based on the detection of the following SNPs; g.16420G>C (G238C, exon 4), g.21147G>A (G460A, exon 6) and g.29,474 A.>G (A719G, exon 9). In order to repatriate a full TPMT pharmacogenetic service to St. James's Hospital, a genetic test has been developed to detect these TPMT mutations.

AIM:

To validate a TPMT genetic test (PCR and Sanger sequencing) using analytical parameters recommended by Eurogentest.

METHOD AND MATERIALS:

Twenty-nine patient DNA samples of known TPMT genotypes (10x TPMT*1*3A, 9x TPMT*1*1, 9x TPMT*1*3C and 1x TPMT*3A*3A) were amplified and sequenced (AB 3730XL sequencer) using the newly developed and optimised TPMT PCR/sequencing primer sets for exons 6 and 9. Lasergene v11.0 software was used to create DNA chromatograms and to align test sequences with the TPMT reference gene (NG_012137.1) respectively. Retrospective assessment of the primer specificity studies of the developmental phase was also undertaken.

RESULTS:

Analytical sensitivity of PCR amplification shows 100% accuracy as the intended DNA target was amplified and 100% trueness as all TPMT amplicons were of expected size. In terms of sequence specificity and analytical sensitivity, full alignment of wildtype DNA samples and human DNA control samples with (NG_012137.1) confirms sequence specificity for all TPMT exons with 100% sensitivity in detection of g.21,147/G460A and g.29,457/A719G SNPs in exons 6 and 9 respectively. A sequence QV score (analytical sensitivity) was pre-set at >30 which has an accompanying <0.1% probability of error. Uncertainty of measurement was measured as <0.1% probability of error of obtained sequence with gross indels not detectable. Reportable range and limit of detection was determined as the genomic location where a consensus of good quality sequencing reads commenced for each coding exon.

CONCLUSION:

The assay correctly identified g.21,147/G460A and g.29,457/A719G positive samples and known wild-type samples tested negative for g.21,147/G460A and g.29,457/A719G. Preliminary data shows an acceptable analytical sensitivity and specificity in the determination of TPMT*1*3A, TPMT*1*1, TPMT*3A*3A and TPMT*1*3C genotypes which is extendable to TPMT*3B. Analytical validation is ongoing with a cohort of 21 blinded patient samples. TPMT*2 samples must be acquired to complete validation.

Clinical sensitivity and clinical specificity should be measured in line with TPMT phenotyping.

Poster 19

Genetic Test for Ferroportin Disease: From Good to Better

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INTRODUCTION:

Ferroportin disease is an autosomal dominant iron overload condition and is the second most common form of hereditary haemochromatosis. Ferroportin protein is the cellular exporter of iron. It is encoded by the gene SLC40A1 in which a large number of causative mutations have been identified.

In this laboratory, a mutation scanning assay based on PCR and direct nucleotide sequencing was previously developed for the detection of ferroportin disease. In line with best-practice guidelines (Eurogentest), continual validation of assays is required. PCR/Sequencing primers should be periodically assessed to ensure on-going optimal performance by checking for newly identified SNPs which may impair primer annealing and assay performance.

AIM:

To perform a retrospective analysis of pre-designed primers and to re-design PCR/sequencing primers where deemed necessary according to best practice guidelines.

MATERIAL AND METHODS:

A retrospective validation of previously designed PCR/sequencing primers was performed which comprised of mapping primer sequences onto the SLC40A1 reference gene (http://www.ncbi.nlm.nih.gov/nuccore/ng_009027) to ensure full coverage of coding sequence regions. Primer locations on reference gene were interrogated for presence of known SNPs and Primer-3 BLAST was performed to confirm target specificity of primers. Eight PCR/Sequencing Primers pairs were then re-designed for all eight exons using Primer 3 BLAST. Human anonymised DNA controls were used in the optimisation of PCR conditions (annealing temperature and time, MgCL₂ concentration and elongation time), and in primer specificity studies

Sanger sequencing was performed and raw sequencing data was analysed using Lasergene® v11.0 software. (Seqman-Pro module was used to create DNA chromatograms and MegAlign was used in order to confirm primer specificity by aligning test sequences against the reference gene).

RESULTS:

Retrospective validation showed that previously designed primers were complementary to SNPs present on NG_009027.1. These primers were functional for the amplification of intended product. However, the sequencing primers for exons 2, 4, 6 and 7a, were originally designed too close (circa 50bp) to the start of the exon for complete coverage of sequence in one forward sequence read. New PCR/sequencing primers were designed to ensure entire coverage of single coding exons by extending the DNA target into intronic areas. Primer specificity of newly designed primers was shown to be optimal by Primer 3 BLAST software and alignment of sequence data to NG_009027.1.

CONCLUSION:

A mutation scanning assay for the detection of ferroportin disease was successfully re-designed in accordance with best practice guidelines. Analytical validation of this assay is ongoing. The new assay should be more cost effective as the need for two sequencing reads to ensure full coverage of an exon has been eliminated.

Poster 20

Development and validation of mutation scanning assays for Autosomal Dominant Hypercholesterolaemia related to mutations in LDLR and PCSK9

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BACKGROUND:

Familial hypercholesterolaemia (FH) is an autosomal dominant disorder due primarily to mutations in LDLR, APOB and less commonly PCSK9. It is characterised by abnormally high concentrations of low density lipoprotein cholesterol, predisposing to premature coronary heart disease and death, but despite its high prevalence many FH patients remain undiagnosed. It is now readily acknowledged that a cascade screening programme based on genetic diagnosis offers the best opportunity for identifying affected patients. Currently there is no clinical diagnostics laboratory providing a direct FH mutation detection service in the Republic of Ireland. This clearly limits the potential to operate an effective cascade screening programme for this condition.

OBJECTIVE:

To establish a comprehensive and robust mutation scanning/screening assay for autosomal dominant hypercholesterolaemia, due to LDLR and PCSK9 mutations.

RESULTS:

PCR and sequencing primer selection was undertaken using both established and in-silico methods. PCR and direct sequencing conditions were optimised and verified, and Lasergene software was used to analyse sequences. Clinical validation was performed by an initial operator blinded study followed by a more extensive study using nine patients referred from Lipid Clinics with a putative diagnosis of FH. Five different mutations in LDLR were identified in six different patients (p.Cyst677Arg, p.Arg633Cyst, p.Asp227Glu, p.Trp4X, c.1478_1479delCT). A method comparison was undertaken for three mutations using Randox biochip array, with full concordance. The mutation D374Y in PCSK9 was not detected in our cohort of nine patients. Assay reproducibility and repeatability for LDLR and PCSK9 was determined using replicate analyses of known genetic variants.

CONCLUSION:

A comprehensive, robust and clinically validated mutation scanning assay for autosomal dominant monogenic hypercholesterolaemia has been established in St James's Hospital. Therefore, this service represents an opportunity to enhance FH diagnosis in Republic of Ireland.

Poster 21

Development and Validation of Mutation scanning assays for the non-acute Erythropoietic Protoporphyria (EPP) & Familial Porphyria Cutanea Tarda (f-PCT) related to mutations in the FECH and UROD genes

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BACKGROUND:

The Porphyrrias are a group of mainly inherited disorders that result from partial deficiency of individual enzymes in the haem biosynthesis pathway. They are commonly divided into either acute and non-acute porphyrias based on clinical presentation. The non-acute porphyrias present with cutaneous photosensitivity characterised by skin lesions, with an absence of acute neurovisceral attacks. The most prevalent of the non-acute inherited porphyrias are porphyria cutanea tarda (PCT) and Erythropoietic Protoporphyria (EPP). While PCT is primarily an acquired disorder up to 20% of cases have familial PCT (fPCT) an autosomal dominant disorder due to mutations in UROD. EPP is an autosomal recessive disorder, in which most patients are compound heterozygotes for a hypomorphic common low expression allele IVS3-48C>T and a loss of function FECH mutation. While biochemical analysis is essential in establishing a diagnosis of PCT or EPP, genetic diagnosis has an important role in identifying presymptomatic carriers of these diseases.

OBJECTIVE:

To establish a mutation scanning assay for EPP and fPCT due FECH and UROD mutations respectively.

RESULTS:

PCR and sequencing primer selection was undertaken using both established and in-silico methods. Extensive optimisation of PCR and direct nucleotide sequencing methods and reaction conditions was undertaken for each coding region of UROD and FECH. Clinical validation was performed on DNA samples from patients with clinical and biochemically confirmed EPP or PCT. Three Pathogenic mutations were identified among the 4 patients with EPP, (P334L, K379X, c.463+1G>C) with all patients homozygous for the low expression allele (IVS3-48C>T). Pathogenic mutations were found in 2 out of 4 patients presenting with putative fPCT, (G303S, R144P). Finally, assay reproducibility and repeatability for UROD and FECH was determined using replicate analyses of known genetic variants.

CONCLUSION:

We report the development and validation of robust mutation scanning assays for two non-acute inherited porphyrias, thus enhancing further the facility for porphyria genetic testing in the Republic of Ireland.

Poster 22

A case of Neonatal Diabetes Mellitus responding to Personalised Medicine

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BACKGROUND:

Neonatal diabetes is defined as diabetes developing before 6 months of age with an incidence of 1 in 200,000 live births. The majority of cases have a mutation in the ATP sensitive potassium channel (K-ATP). This channel is composed of a regulatory subunit (SUR-1 sulphonylurea receptor 1, encoded by ABCC8) and a pore forming channel unit (Kir6.2, encoded by KCNJ11) and most patients with K-ATP mutations respond to sulphonylurea.

OBJECTIVES:

To investigate a lack of responsiveness to sulphonylurea in an infant heterozygous for a novel KCNJ11 mutation (W68G).

CASE:

Baby girl born at 37 weeks gestation with severe intrauterine growth retardation. Maternal gestational diabetes in third trimester was diet controlled. Hyperglycaemia was noted on first day of life and the infant was started on insulin.

RESULTS:

Genetic analysis revealed a novel KCNJ11 missense de novo mutation (p.W68G; c.202t>G) in a highly conserved residue. Mutations previously described at this residue (p.W68R and p.W68L) were associated with transient and permanent NDM respectively. Our patient was transferred from insulin to a standard dose of glibenclamide (1mg/kg/day) at 20 days of life but failed to respond. Pharmacokinetic in vitro studies indicated that the mutated channel would be sensitive to sulphonylurea and our patient was successfully transferred on a higher dose of glibenclamide (2mg/kg/day). This resulted in improved HbA1C (51 mmol/mol) and better weight gain within 6 weeks. The higher dose required to achieve a therapeutic response in our patient was likely caused by a polymorphism in the drug metabolising enzyme, CYP2C9.

CONCLUSION:

This case shows the power of personalised medicine to improve treatment options, glycaemia control and quality of life for patients.

Poster 23

An Unusual Cause of Asymptomatic Jaundice and Isolated Hyperbilirubinaemia

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Asymptomatic jaundice is commonly encountered in clinical practice and can be due to a variety of causes. Further investigation, particularly where there is an isolated increase in bilirubin, may include fractionation of serum bilirubin levels to determine if unconjugated or conjugated hyperbilirubinaemia is present. The differential diagnosis in such cases can include inherited disorders of bilirubin metabolism such as Gilbert's syndrome, if unconjugated hyperbilirubinaemia, and Dubin-Johnson and Rotor syndrome, if conjugated hyperbilirubinaemia predominates. We report the investigation of a patient who presented with asymptomatic jaundice associated with isolated hyperbilirubinaemia.

A 50-year old Sudanese woman was referred from Hepatology OPD to the Chemical Pathology metabolic clinic, St James's Hospital, with conjugated hyperbilirubinaemia (serum total and conjugated Bilirubin 142 and 123 μ mol/L respectively). On review she was asymptomatic and clinical examination revealed icteric sclerae. Previous investigation confirmed that her other LFTs were within normal range and she was negative for both viral and autoimmune hepatitis screens. Ultrasound of the liver showed only mild fatty infiltration compatible with NAFLD. Of note, she was initially investigated for jaundice in Libya 23 years previously following her first pregnancy and the jaundice was perpetually present since then. Her family history was significant for consanguinity (as her parents were first cousins) but not for jaundice per se. Amongst the further investigations undertaken in the metabolic clinic a urine porphyrin screen revealed coproporphyrin III levels > 80% of total, which is consistent with Dubin – Johnson syndrome (DJS), an autosomal recessive condition. Confirmation of the diagnosis is currently being pursued through mutation scanning analysis of ABCC2, where to date pathogenic mutations causing DJS have been reported in 17 of the 32 exons of this gene.

While hereditary hyperbilirubinaemias are rare conditions, simple investigations including serum conjugated bilirubin estimation and urine coproporphyrin analysis can facilitate differential diagnosis. Genetic analysis is a useful adjunct to provide confirmatory diagnosis and reassurance to patients.

Poster 24

From discordant thyroid function tests to unsuspected hypopituitarism: how laboratory liaison can aid diagnosis

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Thyroid function tests (TFTs) are labelled discordant when their pattern differs from expected i.e. when thyroid stimulating hormone (TSH) is not raised in the presence of low free thyroxine (fT4) or when TSH is not suppressed with high fT4. Discordant TFTs are common, caused by multiple conditions (e.g. non-thyroidal illness, hypopituitarism, medication side-effects) and assay interferences.

To enhance the laboratory's clinical role in interpretation of discordant TFTs, we introduced a prospective clinical review system. All the abnormal TFT results are reviewed daily by chemical pathology medical staff and discordant TFTs identified. The requesting clinicians are contacted for patient details, medical and medication history.

Over six months (March-September 2014) we analysed 55,477 TFTs. Six patients (1 female, 5 males, aged 27-87 years) with clinically unsuspected hypopituitarism were identified, with following TFT results: fT4 1.5- 9 pmol/L; TSH 0.38-2.25 mU/L; TT4 14.9-49.3 nmol/L. Laboratory medical staff facilitated anterior pituitary testing, liaised with endocrinologists and general practitioners, advised on hydrocortisone replacement and expedited referrals. Panhypopituitarism was diagnosed in two patients, and secondary hypothyroidism and hypogonadotrophic hypogonadism in the other four patients. Underlying pathology was identified as a macroprolactinoma, and a non-functioning pituitary adenoma, with diagnosis outstanding in four cases. Of note, retrospective analysis of available TFTs suggested previous presence of secondary hypothyroidism 1 month to 8 years before diagnosis.

We report on the outcome of a clinical liaison initiative by laboratory medical staff which resulted in the diagnosis of six cases of unsuspected hypopituitarism, some of which had prior secondary hypothyroidism. Symptoms of hypopituitarism are non-specific and easily attributable to psychological issues or stress. Coupled with low prevalence of the condition, the diagnosis is not often considered in general practice. This initiative demonstrates an important added value role for the laboratory in the interpretation of discordant TFTs.

Poster 25

Hyper Ig D Syndrome (HIDS): Diagnostic Pitfalls of Urine Organic Acid Analysis

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INTRODUCTION:

Hyperimmunoglobulinemia D syndrome (HIDS) and mevalonic aciduria represent ends of a clinical spectrum of disease caused by deficiency of mevalonate kinase (MK), the first enzyme of cholesterol biosynthesis. HIDS is a rare autosomal recessive condition characterized by recurrent febrile episodes typically lasting several days, associated with lymphadenopathy, abdominal pain, elevated serum immunoglobulin D (IgD) levels and elevated urinary mevalonic acid (MVA).

OBJECTIVES:

We present a 4 year old girl of Polish origin who presented at 1 year of age with recurrent febrile episodes lasting 3-4 days approximately every 2 weeks. Fevers were associated with abdominal pain, headaches, arthralgia, cervical lymphadenopathy and hepatosplenomegaly. Extensive investigations were notable for marked elevation of inflammatory markers but no demonstrable infections.

RESULTS:

Immunological work-up demonstrated persistently markedly elevated serum IgD >660 kU/L [reference range 2-100]. Urine organic acid analyses, when afebrile and asymptomatic, demonstrated small peaks of mevalonolactone (MVL) but no MVA. Repeat urine during a febrile episode again demonstrated increased MVL but no MVA. PCR and automated sequencing of the MVK gene on Chromosome 12 demonstrated 2 pathogenic mutations confirming the diagnosis of the HIDS form of MK deficiency. Her parents are compound heterozygotes for the respective mutations.

CONCLUSIONS:

Absence of urinary MVA or MVL does not rule out HIDS. MVA was not detected on GC/MS urine organic acid analysis and MVL excretion was very low in the present case of HIDS. The sensitivity of general organic acid analysis is inadequate for recognizing very low concentrations of MVA present. Detectable urinary MVL may provide a clue to the diagnosis of HIDS and perhaps milder forms of MK deficiency. Detection of urinary MVL in children with recurrent febrile episodes without apparent focus of infection should prompt referral for work-up that includes measurement of serum IgD and molecular genetic analysis for hereditary fever syndromes.

Poster 26

Transcription free integration between an ABSciex LC MS-MS API 3200 and the iSOFT Telepath system for routine Vitamin D Analysis

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OBJECTIVES:

ABSciexQQQMS systems are being routinely used in pathology laboratories to screen for Vitamin D in plasma samples for suspected Vitamin D deficiency or related conditions. Birmingham Heartlands Hospital purchased an ABSciex 3200 LC-MS/MS instrument in 2005 to provide the necessary sensitivity to perform this assay and detect both Vitamin D2 and D3 forms as an alternative to the existing lab approaches. Since then the number of Vitamin D diagnosis requests has grown and now exceeds 25,000 per annum with the instrument in almost continuous use.

STUDY DESIGN:

To maintain our analysis service we looked at all aspects of the Vitamin D assay to increase efficiency, reviewing instrument related parameters such as column types, solvent mixes and gradients and sample preparation protocols. In 2010 we purchased a Tecan Evo robot to automate sample preparation and extraction protocols.

RESULTS:

Once these changes were in place the remaining rate determining step in delivering our overall service to clinicians and patients was the efficient and accurate transmission of completed and verified results. iSOFT's Telepath LIMS/LIS database system is used to request tests and transmit results to users. It operates 24x7 and routinely processes 1,000,000 samples per year. Taking a closer look at sample and result administration workflows and interactions with Telepath, we found that analysts spent three hours per day per instrument run carrying out keyboard/manual transcriptions between different computer systems and paper.

CONCLUSION:

We addressed this remaining facet of our routine Vitamin D workflow by implementing an error and transcription free transfer of all of our Vitamin D results to Telepath. This is done with minimal analyst intervention by making use of barcode labels, Tecan Evoware and ABSciex Analyst software packages, in combination with CSols Links for LIMS instrument integration program and Aqtools charting software for AQC analysis.

Poster 27

Improving turnaround times for trace element screening of hip replacement patients using the CSols Links for LIMS system with a Thermo Scientific X Series ICP-MS Mass Spectrometer linked to a ClinisysWinPath LIMS system

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OBJECTIVES:

Supra-Regional Assay Service, Guildford routinely carry out a wide range of trace element testing and scaled up their facilities to address the increase in testing resulting from the MHRA alert. Improvements were made not only to the method and equipment used for analysis but also to the result delivery service. CSols Links for LIMS software was used to electronically report results to the WinPath LIMS system to maintain a high service level to all submitting clinicians across the UK.

STUDY DESIGN:

CSols Links for LIMS software was installed onto a networked laboratory workstation PC connected to two ThermoFisher X Series ICP-MS instruments running PlasmaLab software. A uni-directional data connection was used via the Siemens Centralink middleware and associated server which was also supporting clinical analyser connections to the Surrey Pathology Services ClinisysWinPath LIS/LIMS.

RESULTS:

Routine Vitamin D workflow was significantly improved and the scale up and improved delivery service were met by implementing an error and transcription free transfer of all of our Vitamin D results to Telepath. This is done with minimal analyst intervention by making use of barcode labels, the Tecan Evoware and AB Sciex Analyst software packages, in combination with the CSols Links for LIMS instrument integration program and Aqtools charting software for AQC analysis.

CONCLUSIONS:

Supra-Regional Assay Service Improved turnaround times for trace element screening of hip replacement patients by using CSols Laboratory Software to integrate instruments, middleware and hospital LIMS system.

Poster 28

Can Harmonised Reference Intervals be Applied in Ireland?

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BACKGROUND:

The use of different reference intervals (RIs) for common Clinical Chemistry analytes is a source of confusion and annoyance for users of laboratory services and could constitute a risk for misdiagnosis.

OBJECTIVE:

To collect data on RIs from clinical chemistry laboratories in the Republic of Ireland, and to determine if harmonised ranges could be applied throughout this health system for ten selected analytes.

STUDY DESIGN:

1. Data Collection. Each laboratory's reference intervals and their sources were collected and anonymised (Survey Monkey questionnaire).
2. Data analysis. All RIs were graphed and commonality and differences reviewed; harmonised RIs were agreed.
3. RI Verification. Plasma or serum from normal individuals was distributed to eight hospital laboratories (n=20/hospital).

RESULTS:

The survey demonstrated considerable variation in reference intervals (RIs) quoted for each analyte, even for different laboratories using the same analyser. From data collected, plus international agreed intervals, the following ranges were proposed: Na 135-145 mmol/L, K 3.5-5.3 mmol/L (serum), urea 2.5-7.8 mmol/L, Cl 95-108 mmol/L, Bicarbonate 22-29 mmol/L, PO₄ 0.8-1.5 mmol/L, Mg 0.7-1.0 mmol/L, Albumin 35-50 g/L (BCG), Total Protein 60-80 g/L, Osmolality 275-295 mmol/L.

Verification studies showed that the proposed RIs were valid except for Bicarbonate and Osmolality. Expected differences were verified for serum versus plasma (K, PO₄, TP) and BCG versus BCP Albumin. Discussion: 9/10 ranges proposed are identical to Pathology Harmony UK. For Sodium we propose a reference interval of 135-145 (Pathology Harmony = 133-146), as used in New Zealand's harmonisation. Lack of sample stability is likely to have affected bicarbonate in the study.

CONCLUSIONS:

- For nine selected routine analytes we propose national adoption of harmonised reference intervals for serum assays.
- In this study eight hospitals, using seven different analysers, verified these assays (CLSI criteria).
- Based on our study findings, we do not support a harmonised RI for Osmolality.
- The impact of plasma versus serum and BCP versus BCG on proposed RIs is the subject of further study.

Poster 29

An E-alert System for Early Detection of Acute Kidney Injury in Hospitalised Patients

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This study aims to retrospectively examine one month's creatinine results from Tallaght Hospital to evaluate the prevalence of AKI in an Irish Population and how we compare to other international studies and to develop an AKI e-alert on the laboratory report to aid diagnosis of AKI earlier as the benefits of earlier detection have been widely reported.

During October 2013, 4202 in patients were admitted to Tallaght Hospital (excluding Dialysis as a source). Microsoft Excel devised rules were applied to alert for AKI, using a change in creatinine results over 48 hours or 7 days, according to KDIGO guidelines. A clinical survey uses the recorded data from the patient's charts to gather relevant information of how they proceeded through the hospital system.

The AKI alert applied to 13% of inpatients which corresponds to other international studies. The range of clinical presentation varied widely from respiratory to psychiatric, indicating it is a hospital wide issue.

Patient's ages ranged from 16-96. The mean age was 69 and with 75 % >60 years old. AKI was only mentioned in 39 (18%) of AKI alert positive patients medical records.

The mean length of stay was 22.5, 32.5 and 68.3 days in those patients with AKIN 1, 2 and 3 respectively. 37% of patients with AKIN3 had no referral to Nephrology even though NICE guidelines say all AKIN3 patients should have referral within 24 hours.

AKI is a serious issue in our health system and is a more prominent problem than previously anticipated. Awareness and detection techniques that are currently in use for AKI are inadequate. The proposed inclusion of an AKI e-alert, awareness campaign and educational bundle, in particular the one page protocol into our everyday hospital practices, should lead to increased awareness, detection, improved care with better outcomes for patients.

Poster 30

Sensible Test Ordering Practice in an Emergency Department

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Inappropriate use of diagnostic laboratory services, particularly over-ordering, can result in diagnostic error, poor patient outcomes and experience, as well as increased costs and waste of hospital resources.

Our aim was to encourage Sensible Test Ordering Practice to reduce the requesting of selected pathology tests by 50% in the Emergency Department of a large Irish teaching hospital by the end of April 2014. We focused on a range of clinical chemistry and haematology tests including coagulation screens, blood glucose, and c-reactive protein.

We used the “S.T.O.P. and think!” technique successfully developed in 2004 in Sydney, Australia, and published in 2013 as the influential Guideline for Pathology Testing in the Emergency Department by the Royal College of Pathologists of Australasia and the Australasian College for Emergency Medicine.

Baseline data on tests ordered were collected and analysed. A working group that included all stakeholders was established. Measurement commenced in January 2014 and consisted of an annotated run chart with results provided weekly to the Emergency Department staff. Other measures included process mapping and observation, a staff satisfaction survey, an analysis of cost savings achieved, and an assessment for any changes in patient length of stay as a result of the interventions.

Plan-Do-Study-Act cycles were conducted around five interventions;

- (1) education at induction,
- (2) scheduled teaching sessions,
- (3) development of a visual aid for guidance in test ordering,
- (4) improved test turnaround time, and finally
- (5) redesign of the pathology test ordering panels on the electronic ordering system which turned out to be the critical intervention

Our aim was achieved after 4 months and 5 cycles, with a 50% reduction in coagulation screens, 98% reduction in blood glucose tests, and significant reductions in several other pathology tests. We also confirmed that patient length of stay was not adversely affected by the reduction in pathology testing.

This project demonstrated that successfully reducing unnecessary pathology testing in Emergency Departments is possible using the tools of quality improvement following identification and careful selection of the optimal intervention.

Poster 31

POCT in Action: Addressing Inpatient Glycaemic Control with an Automated Inpatient Glucometry Alert System

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BACKGROUND:

Poor inpatient glycaemic control has a prevalence exceeding 30% and results in higher rates of hospital complications, increased length of stay and likelihood of readmission and significantly higher inpatient mortality. Current networked Point-of-Care technology offers a novel way to address this problem. The aim of this study was to improve inpatient glycaemic control by developing an automated system to process Point-of-Care Testing Blood Glucose (POCT-BG) results stored on our network server and to alert the Diabetes Consult team about patients with out-of-control results.

METHODS:

Microsoft® Excel® (v 2013) Macros were developed for the processing of daily glucometry data downloaded from the Cobas® IT database. Reports were generated according to ward location and alerts were triggered for any value less than 4 mmol/L (70 mg/dL, hypoglycaemia) or greater than 15 mmol/L (270 mg/dL, moderate-severe hyperglycaemia). The Diabetes Team provided a weekday consult service for all patients flagged on the daily reports. Alerts were also uploaded to the Laboratory Information System. This system was implemented on April 11th, 2014 for a 60-day period. Data were analyzed in Stata®.

RESULTS:

Only inpatient, non-acute, non-paediatric wards were included in the analysis. The baseline mean POCT-BG for our hospital was 9.13 mmol/L with about 12% of values greater than 15 mmol/L and 4% of values less than 4 mmol/L. The alert system resulted in a statistically significant 20% reduction in the percentage of hyperglycaemic patient-day weighted values >15 mmol/L compared to the pre-implementation period without a significant change in the percentage of hypoglycaemic values. The time to next reading after a dysglycaemic POCT-BG result was reduced by 14% and the time to normalization of a dysglycaemic result was reduced from 10.2 hours to 8.4 hours.

CONCLUSION:

The Glucometry Alert System reduced the percentage of hyperglycaemic patient-day weighted glucose values and the time to normalization of blood glucose.

Keywords: Glucometrics, point-of-care testing, glycaemic control, dysglycaemia.

Poster 32

Minimum re-test intervals- An audit of laboratory testing of thyroid function & HbA1c

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OBJECTIVES:

To look at two common biochemical tests (TFT & HbA1c) and assess the appropriateness of testing in the Southern Trust. The goal is to raise awareness of recommended re-test intervals and cut down on unnecessary lab testing.

STUDY DESIGN:

The final 100 HbA1c and 100 TFT samples sent to Craigavon Hospital laboratory in April 2014 were included in this study. The physicians requesting the tests were contacted and asked to provide information on why the sample was requested. The previous patient result was then checked on the hospital computer system and the re-test interval calculated. The results were then analysed and compliance measured against the recommended re-test interval published by the Royal College of Pathologists.

RESULTS:

TFT: 69 respondents. Indications: 23.1% new diagnosis of hypothyroidism; 14.4% monitoring of long term hypothyroidism & 14.4% routine testing. 40.6% of samples sent to the lab did not meet the recommended minimum re-test interval. HbA1c: 72 respondents. Indications: 40.2% looking for a new diagnosis, 41.7% for routine diabetic review. 40% of samples for routine review did not wait the recommended 6 months.

CONCLUSIONS:

Looking at just two common lab tests it is clear many more samples are sent than necessary; this is a waste of time, money and resources. Raising awareness of minimum re-test intervals can help guide physicians and limit their investigations. Other strategies such as splitting thyroid function testing into separate requests for TSH and fT4 will also help in the goal of cutting the work load and costs to both doctors and lab staff.

Poster 33

Establishment and Validation of a Liquid Chromatography-Tandem Mass Spectrometry Method for the Quantification of Free Urinary Metanephrines

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OBJECTIVES:

Phaeochromocytoma is a neuroendocrine catecholamine producing tumour which arises in adrenal chromaffin cells. It is a rare disease which has potentially fatal consequences. The catecholamines (adrenaline and noradrenaline) are metabolised to metanephrines (metanephrine [MN] and normetanephrine [NMN]) at the tumour site and these are released into the circulation. The metanephrines are subsequently conjugated to sulphate in the small intestine. The most commonly used biochemical test for diagnosis of phaeochromocytoma is 24-hr urinary total or fractionated metanephrines. These are measured after an acid hydrolysis step that releases the free metanephrines from the sulphur-conjugated metabolites. Recent work speculates, however, that measurement of the free pre-conjugated metanephrines may better reflect the dynamics of catecholamine production by tumour cells. In this work we describe and validate a new assay for free urinary metanephrines developed by AB SCIEX for liquid chromatography tandem mass spectrometry (LC-MS/MS).

STUDY DESIGN:

Urine samples were extracted by reverse phase ion chromatography, dried down and resuspended. The metanephrines were analysed by LC-MS/MS using positive electrospray ionisation and multiple reaction monitoring following separation by ultra fast liquid chromatography using a HILIC column. The validation carried out included studies of linearity, intra- and inter-assay precision, accuracy, recovery studies, signal to noise ratio (S/N), method comparison and reference interval establishment.

RESULTS:

Retention time for MN was 3.62 min and 3.66 min for NMN. The assay was linear to a concentration of 5000 ng/ml ($r^2 > 0.999$). Interassay precision was 3.2% and 3.4% for metanephrine and normetanephrine respectively. Intraassay precision was 8.5% and 6.7%. Accuracy studies relative to known concentrations of MN and NMN demonstrated CVs of 7.6% and 11.5% respectively. Average recoveries for MN were 88% and 98% for NMN. S/N was well in excess of acceptable (MN 218, NMN 68). Method comparison between a HPLC urinary fractionation assay and the free metanephrine assay under investigation yielded highly significant correlations ($r^2 = 0.6735$; MN and $r^2 = 0.7432$). Reference ranges were calculated using urine samples from healthy individuals with no history of phaeochromocytoma (n = 30). Ranges were 0-69 nmol/l for MN and 0-75 nmol/l for NMN.

CONCLUSION:

The assay is accurate, precise, and linear for the measurement of urinary free metanephrines and demonstrates good correlation with an established HPLC assay for total metanephrines. Both MN and NMN have short retention times and the removal of the acid boiling step would ensure rapid turnaround of results. An assessment of the test's clinical validity is being established to determine its sensitivity and specificity for biochemically diagnosing phaeochromocytoma.







Prostate Health Index (PHI)

Three times more specific in detecting prostate cancer than PSA (prostate-specific antigen).

The Prostate Health Index (PHI) is a mathematical formula that combines total PSA, free PSA and a new serum marker known as [-2] proPSA into a single score that can be used to aid in clinical decision-making, and is estimated to be 3 times more specific in detecting prostate cancer in patients than PSA screening alone¹. [-2]proPSA is strongly expressed in the peripheral zone of cancerous tissues of the prostate and is rarely expressed in the transition zone, which is the main site of most benign prostatic hyperplasia. It is therefore a more specific marker for prostate cancer than PSA.

Clinical Utility of PHI:

-  Outperforms PSA screening in detecting clinically significant prostate cancer
-  Significant correlation between PHI and the Gleason score²
-  Reduces the occurrence of unnecessary prostate biopsies³
-  Helps to avoid negative prostate biopsies, thus reducing direct costs⁴

If you would like further information about this test please contact our Sales Department on (01) 295 8545 or email us at sales@biomnis.ie. You can also find out more about this test on-line at: www.biomnis.ie.



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