

ACBI 2017

40TH Annual Conference

Association of Clinical Biochemists in Ireland



**THE ARDILAUN HOTEL
GALWAY**

**Friday & Saturday
November 10th & 11th**

2017



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Welcome to...



Proceedings of
40TH Annual Conference
Association of Clinical Biochemists in Ireland

**The Ardilaun Hotel,
Galway**

November 10th & 11th, 2017

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A message from the President of the ACBI

Professor Maria Fitzgibbon
President, ACBI



I have great pleasure in extending a warm welcome to all the participants at the 40th Annual Conference of the Association of Clinical Biochemists in Ireland (ACBI) in Galway, 2017.

Our programme this year addresses the diagnosis and management of neuroendocrine tumours (NETS), the abnormalities in the cell and its components, and their involvement in metabolic diseases. This truly highlights the skills of clinical biochemists where basic science meets clinical medicine, when deranged cellular components are identified in the diagnostic laboratory to be causative of disease. In keeping with the evolving role of biochemical genetics, we look forward to hearing how whole exome sequencing (WES) will not replace, but complement biochemical pathway investigations.

Drug misuse and addiction is an ever increasing and topical issue in life and in international sports. What has he/she taken? is generally high up in the list of differential diagnoses and there is an onus on the diagnostic laboratory to keep pace with the evolving drug culture from steroids to crystal meth, opioids and a very long list of others.

All aspects of our profession from Trainee Clinical Biochemists to Consultants have input to making this an exciting scientific and clinical conference. Our Trainees will present short cases and updates and our research hotspot provides a brief insight into progressive translational research.

In the past year we have had success in attracting new members and Trainees educated through world-class universities in Ireland and UK and our clinical biochemistry training programme is building competencies and progressing well.

The fight for limited resource within the HSE is always difficult with so many demands for new drugs, new technology, etc. but we have to continue to prove that clinical biochemistry and diagnostic medicine is essential for all patients now and into the future. We punch above our weight to implement new technological advancements including mass spectrometry, next-generation sequencing, proteomics, with limited budgetary and staff resource so as to drive today's scientific developments to be tomorrow's patients standard norm.

To our national and international, laboratory and clinical colleagues I look forward to a successful few days of inspiring exchange of medical and scientific knowledge and some enjoyable food and drink collaborations.

Galway Bay



Céad Míle Fáilte

Welcome to ACBI 2017

On behalf of the organising committee, I wish to extend **Céad mile fáilte romhat** at this the 40th Annual Conference of the Association of Clinical Biochemists in Ireland (ACBI). I am particularly delighted to welcome you to the West of Ireland and the beautiful harbour city of Galway, the chosen venue for this year's Conference. On behalf of the ACBI, I particularly wish to acknowledge and extend our thanks and appreciation to our colleagues from the diagnostic industry without whose on-going support this conference would not be possible.

This year's scientific programme is a whirlwind of medicine and clinical biochemistry. On Friday morning the challenging area of neuroendocrine tumours is presented together with current biochemical investigation strategies and novel diagnostic developments. This is followed in the afternoon with presentations on a new genetic-testing approach to the investigation of inherited metabolic disease. Both sessions will be peppered with case vignettes and conundrums. After such a demanding day, I guarantee it will be a case of **Eat Feast & be Merry**. Here, I must caution moderation as Saturday's programme promises to be highly stimulating. All things chemical in fact! – from steroids in sport to toxicology in the Emergency Department and in the Coroner's Autopsy – not forgetting those "legal highs". After coffee the presentations continue with topics on translational research followed by a light-hearted *Did you know?* and "myth busting" session.

Finally, and prior to the conference close, the medals for the best basic science and clinical case posters will be presented.

I hope that by now this whistle stop synopsis has adequately whetted your appetite for learning? May I take this opportunity again to wish you, our invited speakers and guests a highly educational, exciting, and successful ACBI conference 2017.

Dr. Paula O'Shea
Chairperson ACBI 2017 Organising Committee



Continuing Education

Royal College of Pathologists

ACBI 2017 Conference has been approved for 9 CPD credits by the Royal College of Pathologists.

Medical staff and clinical scientists in career grade posts who are enrolled with one of the Royal Colleges for CPD purposes and attend the meeting will be entitled to receive CPD credits.

Academy of Clinical Science and Laboratory Medicine

This meeting is accredited with 5 CPD credits for attendance on Friday and 4 credits for attendance on Saturday

ACBI CPD Scheme

The ACBI CPD scheme awards one credit per hour for attendance at conferences.

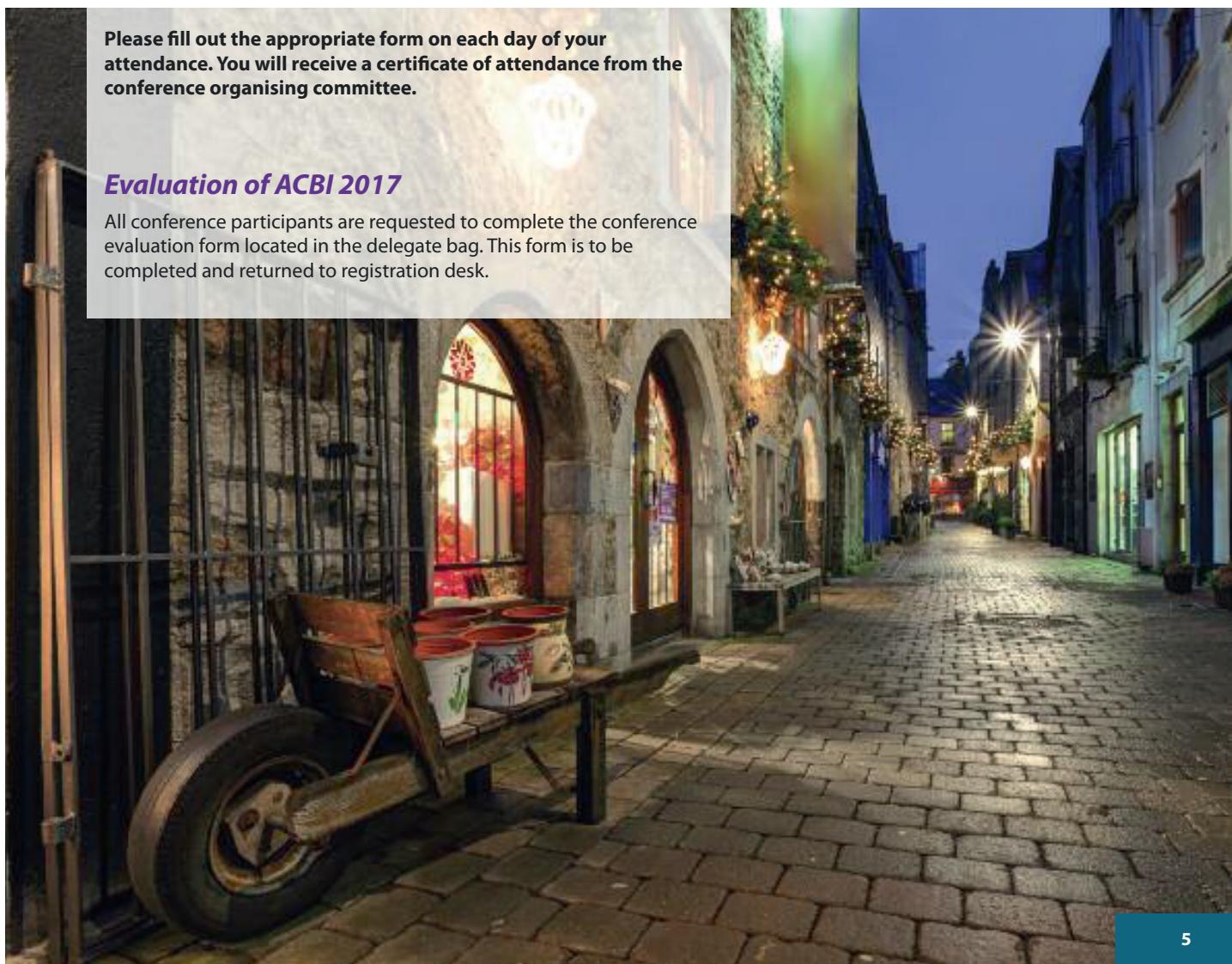
The facility to collate your personal CPD is available on the member's area of the ACBI website.

Galway Street

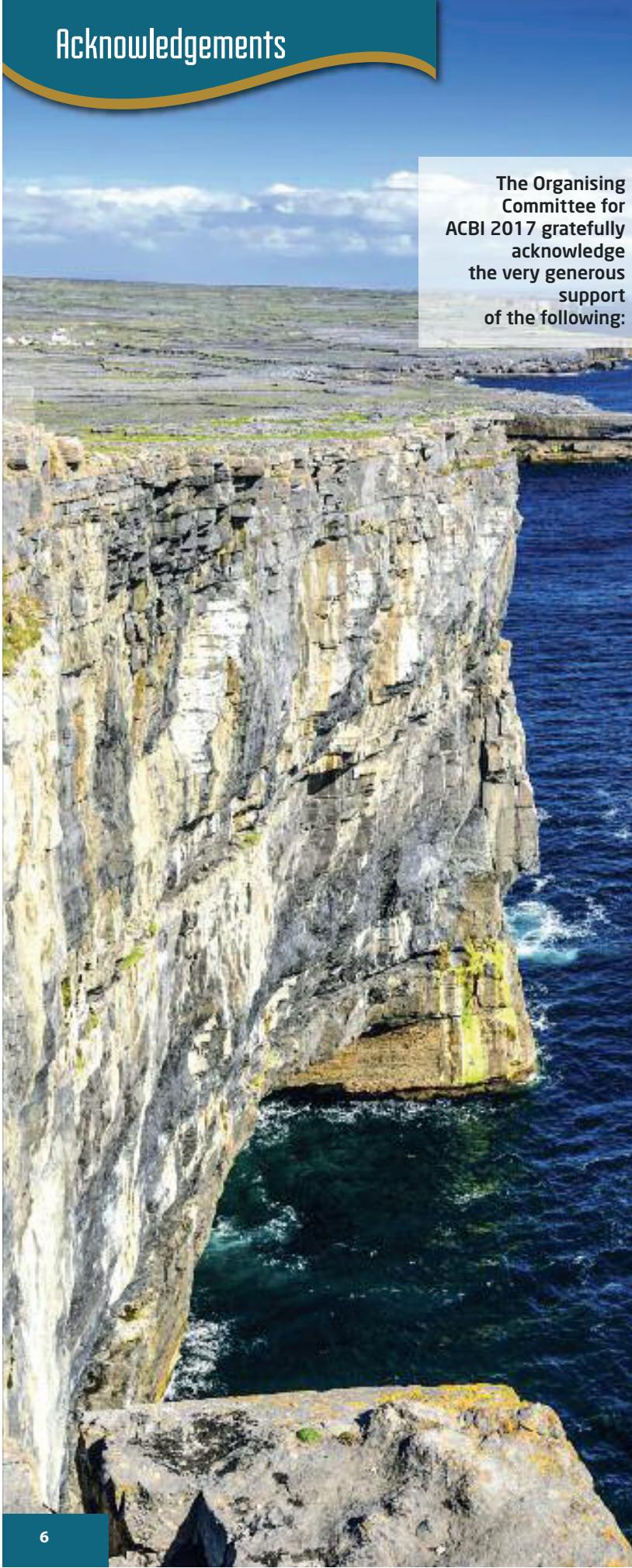
Please fill out the appropriate form on each day of your attendance. You will receive a certificate of attendance from the conference organising committee.

Evaluation of ACBI 2017

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



Acknowledgements



The Organising Committee for ACBI 2017 gratefully acknowledge the very generous support of the following:

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Mater Misericordiae University Hospital
Dr. Maria Fitzgibbon
Dr. Graham Lee

Cork University Hospital
Ms. Caroline Joyce

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Programme

Conference Opening

09.00	Registration and Coffee
10.00-10.15	Opening Remarks – Prof. Maria Fitzgibbon, ACBI President

Session 1: Friday Morning Neuroendocrine Tumours

Chair: Dr Paula O'Shea



10.15-10.45	A study of SDH deficient tumourigenesis: 'From functional assessment of VUS to discovery of new disease biomarkers and potential therapeutic targets' Dr. Ruth Casey Clinical Research Fellow, University of Cambridge.
10.45-11.15	Whistle stop tour: Biochemical investigation of NETs Dr. Tricia Tan Consultant in Diabetes, Endocrinology and Metabolic Medicine, Imperial Health London
11.15-11.45	Coffee and Poster Viewing
11.45-12.15	Update on the biochemical investigation and monitoring of Carcinoid Tumours Dr. Brendan Byrne Senior Clinical Biochemist, Beaumont Hospital, Dublin
12:15-12:45	MEN: A family affair Dr. Marcia Bell , Consultant Endocrinologist, University College Hospital Galway
12:45	Lunch and attended Poster Session



Session 2: Friday Afternoon Cell Biochemical Metabolism

Chair: Prof. Maria Fitzgibbon



14.00-14.30	Whole Exome Sequencing – A New approach to the Investigation of Inherited Metabolic Disease Dr. Tony Marinaki , Consultant Clinical Scientist, St. Thomas's Hospital, London
14.30-15.00	Genotype phenotype conundra Prof. Simon Heales Professor of Clinical Chemistry, ICH Genetics & Genomic Medicine, University College London
15.00-15.15	Prof. Jo Martin , President-Elect, Royal College of Pathologists (UK)
15.15-15.45	Coffee and attended Poster Session
15.45-16.15	Differential Diagnosis of Hyperammonaemia Dr. Ingrid Borovickova Consultant Chemical Pathologist, Temple Street Children's University Hospital
16.15-16.45	Genetic Diagnosis of Mitochondrial Disorders Dr. Carl Fratter Principal Clinical Scientist, Oxford University Hospital



Programme

16.45-17.15 **Newborn Screening in Northern Ireland – where are we now and where are we headed to?**
Dr. Jennifer Cundick
 Consultant Clinical Scientist, Royal Group of Hospitals Belfast

Friday Evening

19.00 Drinks Reception



20.00 Annual Dinner

Saturday

8.30-9.30 **ACBI AGM (Ordinary members only)**

Session 3: Saturday

Chair: **Dr. Graham Lee**



9.45-10.15 **Use, misuse and abuse of steroids in sport**
Prof. David Cowan
 Director, Drug Control Centre, King's College London

10.15-10.45 **Toxicology in the Emergency Department**
Dr. Conor Deasy
 Consultant in Emergency Medicine Cork University Hospital

10.45-11.15 **Biochemical investigation of legal highs**
Dr. Loretta Ford
 Consultant Clinical Biochemist, Birmingham City Hospital

11.15-11.45 Coffee and attended Poster Session

Session 4: Saturday

Chair: **Dr. Damian Griffin**



11.45-12.15 **The three-legged stool – The role of Toxicology in the Coroner's Autopsy**
Dr. Margot Bolster
 Assistant State Pathologist

Clinical Translational Research Hotspot

12.15-12.45 **Insights into beta-cell autoimmunity from monogenic diabetes**
Dr. Matthew Johnson
 University of Exeter

12.45-13.00 **Biomarkers of Targeted Therapy Resistance in Breast Cancer**
Dr. Haley Ellis
 UCD and Sloan Kettering Memorial, NY

Did you know? – Session Moderator: Ms. Caroline Joyce

13:00-13.20 **Quirky enzyme myths and truths** **Micheál Ryan**
Changing the cause of death **Karen Heverin**

13.20-13.30 Awards for Best Poster:
The Geraldine Roberts medal for the best Basic Science Poster.
The ACBI medal for the best Clinical Case Poster.

13.30 Conference Close followed by Lunch



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Your Patients, Our Priority

MESSAGE FROM - Brian Madden, CEO MedLab Pathology



Our Healthcare system and in turn diagnostics are consistently adapting to meet the growing challenges they face. Since our establishment, MedLab Pathology (MLP) has sought to be a support and a leader in diagnostics. By listening carefully to our clients in this ever-changing environment,

we offer innovative solutions and best practice in diagnostics. With these challenges, there is also a shift to provide a '*prevention is better than cure*' approach and as such the diagnostics' role continues to grow in the upkeep of the Health for our populations. This has been achieved in Ireland already in a number of ways including several screening programmes. MLP are proud to be a provider of Pathology Services for the National Cervical Cancer Screening Programme (CervicalCheck) and the National Bowel Cancer Screening Programme (BowelScreen).

MLP continuously evolves to meet client's needs and 2017 has been a very exciting year. New technology brings many diagnostic advantages, most importantly improved patient outcomes. I consider investment in new technologies and increased capacity vital to our Pathology offering. As such we have extensively expanded our auto lab portfolio of tests being run at MLP in Dublin. Also, through client feedback, we expanded our services in January 2017 to offer 24/7 Pathology analysis. With this we have welcomed new

staff into the MLP family. Our performance to date is directly attributable to the loyal and committed efforts from our people. *This growth will continue* in the coming months with an expansion of our Commercial division, innovative ways to allow quick access to referred pathology analysis, further IT investment, expansion of logistics routes and further expansion of our local pathology offerings.

MLP as part of the Sonic Group also has a role to **push the boundaries and innovate**. A recent example of this is Health Service Laboratories-HSL, a UK Joint Venture between TDL (Sonic Healthcare UK), UCLH and The Royal Free London. Together through HSL we provide pathology to the NHS through the delivery of medically-led diagnostics, innovation, value and long-term investment to healthcare. The HSL flagship laboratory, the Halo building, will be transformational in the delivery of a new kind of healthcare.

I firmly believe that with our global hospital laboratory experience and our Medical Leadership culture, we are well placed in offering innovative laboratory management and **Pathology expertise in Ireland**, as well as efficiencies and cost savings moving forward. We fully understand the complexity of the delivery of such a service to you. MedLab Pathology with Sonic Healthcare will continue to provide clinicians with the information that they need to manage patients in a timely and appropriate way, providing the foundation for optimal health outcomes for both the individual as well as the community as a whole.



For More Information on MLP's services please contact our
Sales & Marketing Department on
sales@medlabpathology.ie or **1800 303 349**
 MedLab Pathology Ltd, Unit 3, Sandyford Business Centre,
 Sandyford Business Park, Dublin 18, Ireland.



SONIC
HEALTHCARE

Speakers' Abstracts

Session 1

Neuroendocrine Tumours



Chair:
Dr Paula O'Shea

Dr. Ruth Casey
Clinical Research Fellow, University of Cambridge

**A study of SDH deficient tumourigenesis:
'From functional assessment of VUS to
discovery of new disease biomarkers and
potential therapeutic targets'**

Dr. Tricia Tan
Consultant in Diabetes, Endocrinology and Metabolic
Medicine, Imperial Health London

**Whistle stop tour:
Biochemical investigation of NETs**

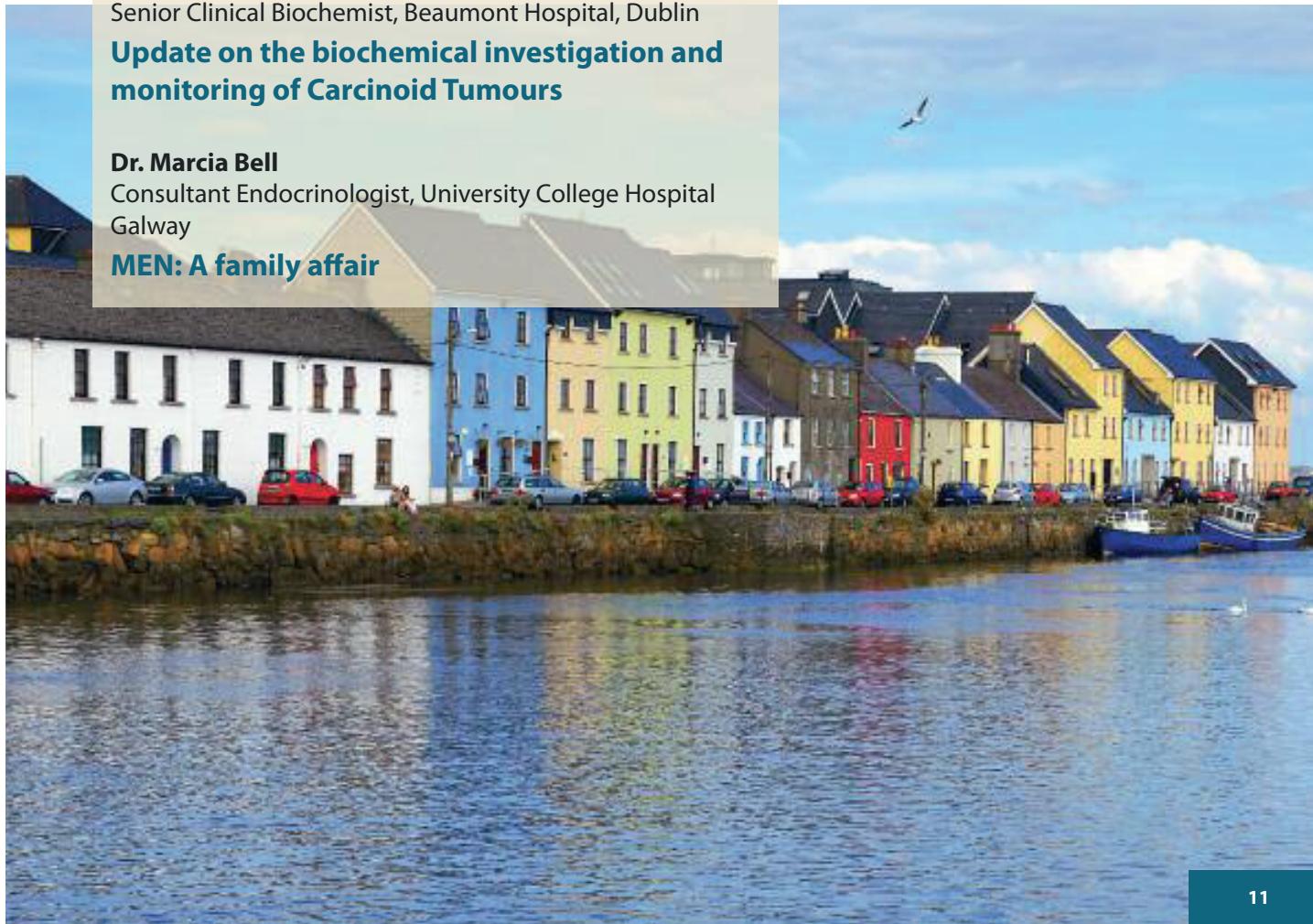
Dr. Brendan Byrne
Senior Clinical Biochemist, Beaumont Hospital, Dublin

**Update on the biochemical investigation and
monitoring of Carcinoid Tumours**

Dr. Marcia Bell
Consultant Endocrinologist, University College Hospital
Galway

MEN: A family affair

Claddagh, Co. Galway



Speakers' Abstracts

Dr. Ruth Casey

MB BCH BAO, RCPI

Clinical Research Fellow,
University of Cambridge.



BIOGRAPHY

Dr Ruth Casey is an Irish endocrinology trainee, who is in the final year of her PhD and higher specialist training scheme. Ruth has a specialist interest in hereditary endocrine neoplasia

and endocrine cancer, nurtured over the course of her clinical training in Ireland.

In 2015, Dr Casey was awarded a PhD Fellowship by the Health Research Board Ireland and this research is taking place under the supervision of Prof Eamonn Maher in the department of Medical Genetics in Cambridge University Hospital.

Her research investigates the role of succinate dehydrogenase gene mutations in tumorigenesis and has a strong translational focus.

Session 1

A study of SDH deficient tumorigenesis: 'From functional assessment of VUS to discovery of new disease biomarkers and potential therapeutic targets'

Mutations in the citric acid cycle enzyme complex succinate dehydrogenase (SDH) are associated with a spectrum of tumorigenesis including phaeochromocytoma¹, paraganglioma¹ (PPGL), gastrointestinal stromal tumours (GIST)², renal cell carcinoma (RCC)³ and pituitary adenomas⁴. Mutations in each of the four genes encoding the four sub-components of this complex (SDHA/B/C/D) have been associated with tumorigenesis. Germline mutations in SDHB account for up to 50% of patients with malignant disease and a 5 year survival of less than 50% in those with malignancy⁵. Mutations in SDH are inherited in an autosomal dominant fashion and carriers of these mutations are recommended to have life-long surveillance using biochemistry and cross sectional imaging techniques⁶. When tumours develop, predicting malignant disease is very difficult and histology is of limited assistance in this prediction.

The advent of next generation sequencing (NGS) has been influential in this field of inherited neoplasia allowing more rapid and accurate identification of mutations, including those in the SDH complex and enables early screening of affected first degree relatives. The increased throughput achieved with NGS methodology has yielded more variants of uncertain significance in these genes which require additional assessment. New diagnostic adjuncts such as SDHB immunohistochemistry⁷, has provided additional prognostic information and prediction of malignant risk but further biomarkers are needed. Furthermore there is a lack of effective treatments for malignant disease associated with SDH mutations^{8,9}. This project aims to investigate mechanisms of SDH-associated tumorigenesis in order to i) identify biomarkers of malignant disease, ii) identify new methods to assess variant pathogenicity, iii) enable better genotype phenotype correlations and iv) to identify potential targeted therapies for this inherited neoplasia syndrome.

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Speakers' Abstracts

Session 1

Whistle stop tour: Biochemical investigation of NETs

My talk will introduce the concept of gut hormones and how they are used as biomarkers for neuroendocrine tumours. This will be followed by some illustrative cases of how we use them in practice and the functional syndromes associated with excessive gut hormone secretion.

Dr. Tricia Tan

**Consultant in Diabetes,
Endocrinology and Metabolic
Medicine, Imperial Health London**



BIOGRAPHY

I qualified in 1996 from University of St Andrews/Manchester and underwent specialist training in Endocrinology and Diabetes, subsequently training in Chemical Pathology. I am currently a Consultant in Metabolic Medicine and Endocrinology at Imperial College Healthcare NHS Trust since 2007, and am the Clinical Biochemistry Lead for NW London Pathology as well as the director of the UK Endocrine SAS Laboratory for Gut Hormones.

My clinical interests are in the diagnosis and management of neuroendocrine tumours. My research has concentrated on characterizing the physiological effects of human gut hormones on appetite, energy expenditure and glucose homeostasis. A major second theme has been the rational design of gut hormone analogues for therapy of obesity and diabetes, and early Phase clinical trials.

Speakers' Abstracts

Dr. Brendan Byrne

**Senior Clinical Biochemist,
Beaumont Hospital,
Dublin**



BIOGRAPHY

Brendan originally studied Biochemistry at the Dublin Institute of Technology during the early 90s. He subsequently moved to St Vincent's University Hospital

and UCD, to pursue a post graduate degree. His dissertation investigated the role played by small intestinal enterocytes in the development of oral tolerance to dietary antigen.

On completion of his PhD, he began working in Beaumont Hospital and has been based there ever since. During his time in Beaumont he has completed an MSc in Clinical Chemistry and the first part of the FRCPath examinations. In his current role, he is the Senior Clinical Biochemist with responsibility for the Neuroendocrine Tumour section.

Session 1

An Update on the Biochemical Investigation and Monitoring of Carcinoid Tumours

The overall aim of this presentation is to give a broad overview of carcinoid tumours / carcinoid syndrome with an emphasis on the biochemistry. The term Carcinoid is generally used when referring to Neuroendocrine tumours originating primarily within the digestive tract or lungs, but occasionally in other sites such as the kidneys and ovaries. Carcinoid syndrome is the term used to describe the characteristic clinical features associated with a subset of patients with Carcinoid tumours. These tumours are generally discovered in either of three ways; i) They are often discovered incidentally during endoscopic procedures, ii) they are suspected on the basis of the Carcinoid syndrome, or iii) when the tumour mass itself starts to cause symptoms such as abdominal pain.

Imaging such as CT and MRI are important in identifying tumour location and any related metastases. From a biochemical point of view there are two stand-out tests used to identify carcinoid syndrome. These are urinary 5-Hydroxyindolacetic acid or 5-HIAA and chromogranin A. 5-HIAA testing is generally a sensitive and specific test for those with the carcinoid syndrome and as such is useful towards an initial diagnosis, whereas its usefulness is low in those with carcinoid tumours without carcinoid syndrome. Thus 5-HIAA cannot be used to rule out the presence of a carcinoid tumour. False positive results are also common as a result of various dietary and medicinal interferences. These factors should be considered in the days prior to urinary collection. There are also several causes of reduced 5-HIAA levels, which are especially important when using the test for an initial diagnosis.

An elevated 5-HIAA is generally associated with tumours of the midgut region. These tumours produce large amounts of serotonin which breaks down to 5-HIAA. However, foregut and hindgut tumours lack the decarboxylase required to convert 5-hydroxytryptophan (5-HT) to serotonin and thus do not produce elevated 5-HIAA. Instead increases in 5-HT may be present.

The chromogranins are proteins stored, and subsequently secreted by a variety of neuroendocrine tumours. Chromogranin A is the most sensitive and widely used assay, but it is not specific for carcinoid tumours. There are a wide variety of common conditions that result in an elevated chromogranin A. Therefore it is not generally considered a useful screen for carcinoid tumours. However, it is particularly useful as a tumour marker in patients with an established diagnosis for monitoring efficacy of treatment, disease progression and recurrence. There are also several potential causes of false positivity that should be excluded. There are a variety of other tests that may be used from time to time. Examples include blood serotonin, platelet-rich plasma serotonin, plasma 5-HIAA and chromogranin B.

On completion of this presentation it will be evident that the biochemical analyses play an important role in the diagnosis and subsequent management of patient's with carcinoid tumours and carcinoid syndrome in particular.

Speakers' Abstracts

Session 1

MEN: A family affair

Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant condition known to predispose to tumours of the parathyroid glands, anterior pituitary, and entero-pancreatic endocrine cells. The clinical spectrum of this disorder has been expanded and it is now known that tumours in the duodenum, adrenal adenomas, carcinoid tumours and lipomas are more common in MEN1 than in the general population.

Managing patients with MEN1 can be challenging and a multidisciplinary approach to management is essential. I will present clinical cases of MEN1 outlining the important collaboration between Clinicians and the Biochemistry department in the diagnosis and management of MEN1.

Dr. Marcia Bell

**Consultant Endocrinologist,
University College Hospital Galway**



BIOGRAPHY

Dr Marcia Bell was appointed as a Consultant Endocrinologist at Galway University Hospital (GUH) in 2007. She has a particular interest in endocrine malignancy and runs a neuroendocrine service at GUH. She completed a Clinical Fellowship (2005-2007) in endocrine malignancy at the Adult Endocrinology unit, St. Bartholomew's hospital, London. Prior to then she held the post of Lecturer in Medicine and Research in Molecular Biology and Gene therapy (2003-2005), at the National University of Ireland, Galway.

Dr. Bell is a graduate of Trinity College Dublin (1996). Following post graduate training in Medicine at the Federated Dublin Voluntary hospitals (1999), she completed Specialist Training; Endocrinology and Diabetes mellitus with the Royal College of Physicians of Ireland (2004).

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Speakers' Abstracts

Session 2

Cell Biochemical Metabolism



Chair:

Prof. Maria Fitzgibbon

Dr. Tony Marinaki

Consultant Clinical Scientist, St. Thomas's Hospital, London

Whole Exome Sequencing – A New approach to the Investigation of Inherited Metabolic Disease

Prof. Simon Heales

Professor of Clinical Chemistry, ICH Genetics & Genomic Medicine, University College London

Genotype phenotype conundra

Dr. Ingrid Borovickova

Consultant Chemical Pathologist,
Temple Street Children's University Hospital

Differential Diagnosis of Hyperammonaemia

Galway Hooker

Dr. Carl Fratter

Principal Clinical Scientist, Oxford University Hospital

Genetic Diagnosis of Mitochondrial Disorders

Dr. Jennifer Cundick

Consultant Clinical Scientist,
Royal Group of Hospitals Belfast

Newborn Screening in Northern Ireland – where are we now and where are we headed to?



Speakers' Abstracts

Dr. Tony Marinaki

*Consultant Clinical Scientist,
St. Thomas's Hospital,
London*



BIOGRAPHY

Tony Marinaki is a Consultant Clinical Scientist in the Purine Research Laboratory, Viapath, St Thomas' Hospital. He has published widely in the fields of

pharmacogenetics and inherited defects of purine and pyrimidine metabolism.

Session 2

Whole Exome Sequencing – A New approach to the Investigation of Inherited Metabolic Disease.

There are more than 500 inherited metabolic diseases. No single biochemical test is able to diagnose the majority of disorders, and as a result, just one third of cases are diagnosed by the age of one year. Limited clinical exome sequencing has the potential to diagnose the majority of genetic disorders in a single test. However concerns about false positives and the cost of pursuing these have delayed the introduction of limited clinical exome sequencing as a first line test.

In a pilot study conducted with the Paediatric Metabolic Disease Unit at the Evelina London Children's Hospital, we showed that limited clinical exome sequencing using the Illumina TruSight One gene panel enabled the diagnosis to be made in eight of nine patients with a known metabolic disorder. In six patients, this was done without clinical or demographic information. After clinical information was provided, the defective gene was identified in two patients. Limited clinical exome sequencing has promise as a first line test for metabolic disorders, and if introduced, will change the way patients are diagnosed. A diagnosis within two weeks for up to 90% of patients is feasible, as opposed to a diagnostic odyssey often lasting years.

Speakers' Abstracts

Session 2

Genotype Phenotype Conundra

Diagnostic laboratories are moving towards a combined omics approach with regards to the investigation of clinical samples. Consequently, clinical samples may be expected to embark on parallel journeys involving genomics, proteomics, metabolomics, fluxomics etc. This with the hopeful aim of generating a comprehensive and digestible report with a clear diagnosis.

In reality, we are not completely there yet. However this approach is inevitable, particularly with regards to patients with complex conditions and where there is considerable overlap of phenotype between the conditions. For disciplines such as enzymology or metabolic profiling, workload is increasing; results from genomic screens are identifying variants of unknown significance with subsequent requests for functional studies. However, the converse is also true, e.g. an abnormal metabolic profile may point strongly to a specific metabolic disease yet the clinical phenotype is atypical. The hope here is that genetic conformation provides the answer.

The interplay between metabolic pathways also needs to be appreciated. Identification of an abnormal metabolite does not necessarily point towards the correct primary metabolic defect, e.g. impaired folate metabolism secondary to a mitochondrial disease. Combined omics will undoubtedly lead to quicker diagnoses of very complex conditions. Additionally, reliable and specific biomarkers will continue to be identified enabling prediction of disease severity and the monitoring of responses to treatment.

Prof. Simon Heales

**Professor of Clinical Chemistry,
ICH Genetics & Genomic Medicine
University College London.**



BIOGRAPHY

Prof Simon Heales completed his PhD at Aston University and is a Fellow of the Royal College of Pathologists. He is the Head of Service for Laboratory Medicine at Great Ormond Street Hospital and holds the UCL Chair of Clinical Chemistry.

He has a strong interest in the diagnosis and monitoring of patients with inherited metabolic disorders. This work is underpinned by a number of basic and translational research projects that are carried out in conjunction with the UCL Institute of Child Health.

He has published over 150 papers in the area of mitochondrial, neurotransmitter and lysosomal disorders. Simon is also the Clinical Lead for the Neurometabolic Unit at the National Hospital, Queen Square (UCLH Foundation Trust).

Speakers' Abstracts

Session 2



Professor Jo Martin

MA MB BS PhD MA FRCPath

President-Elect of the Royal College of Pathologists

Professor Martin Qualified Cambridge University and London Hospital Medical College 1984, MRC Training Fellowship 1988, MRC Fellowship 1990, Wellcome Trust Advanced Research Training Fellowship 1991. PhD in cellular pathology of MND 1997. Kings Fund programme MA in Leadership in 2005.

Jo has over 100 published papers including Nature group and Science journals and is Professor of Pathology at Queen Mary University London. She is a founder of Biomoti, a drug delivery platform technology company, and has created suite of apps including an elearning platform, eCPD

She has very broad experience in healthcare management ranging from running clinical departments and divisions to acting as Medical Director, and subsequently Chief Medical Officer at Barts Health NHS Trust, and covering for the Chief Executive.

As Director of Academic Health Sciences she is responsible for CRN North Thames, hosted by Barts, for research across the Trust and for the training and education of 16,000 staff across Barts Health. Her clinical specialist expertise is in the pathology of gastrointestinal motility disorders.

National Clinical Director of Pathology for NHS England April 2013-16, Jo has worked across a broad range of programmes and projects in all the pathology disciplines including genetics, transfusion, digital pathology, data, networks and working with the diagnostic professional bodies.

Jo becomes President of the Royal College of Pathologists on 16th November 2017.

Speakers' Abstracts

Session 2

Differential Diagnosis of Hyperammonaemia

Dr. Ingrid Borovickova

**Consultant Chemical Pathologist,
Temple Street Children's University
Hospital**

BIOGRAPHY

Consultant Chemical Pathologist, Temple Street Children's University Hospital, Our Lady's Children's Hospital Crumlin and Rotunda Hospital Dublin.

She is director of the National Newborn Bloodspot Screening Programme in the Republic of Ireland.

Speakers' Abstracts

Dr. Carl Fratter

**Principal Clinical Scientist
Oxford University Hospital**



BIOGRAPHY

Carl Fratter is a Principal Clinical Scientist and leads the mitochondrial genetics team within the Oxford Medical Genetics Laboratories. He has specialised in the genetic diagnosis of mitochondrial disorders for over 15 years.

Carl collaborates closely with laboratory, clinical and research colleagues to translate new research findings into diagnostic practice, and to provide an optimal service which is linked to clinical and biochemical services. He has particular interest and expertise in disorders of mitochondrial DNA maintenance and has co-authored several papers in this field. Carl has been a registered as a Clinical Scientist since 2004 and was awarded Fellowship of the Royal College of Pathologists in 2008. Before that he obtained Masters degrees at the University of Oxford and the University of Birmingham.

Session 2

Genetic Diagnosis of Mitochondrial Disorders

Carl Fratter¹, Kate Sergeant¹, Conrad Smith¹, Ruth Brown¹,
Garry Brown¹, Joanna Poulton²

¹ Oxford Medical Genetics Laboratories, Oxford University Hospitals NHS Foundation Trust, Oxford

² Nuffield Department of Obstetrics and Gynaecology, University of Oxford, Oxford

Mitochondrial disorders, due to defects in cellular energy production, are phenotypically and genetically heterogeneous, and hence diagnosis is notoriously challenging. A multidisciplinary approach, including biochemical and genetic investigations, is essential for diagnosis.

At the genetic level, mitochondrial disorders can be classified into 3 categories: primary mitochondrial DNA (mtDNA) disorders, mtDNA maintenance disorders, and nuclear gene disorders with no effect on mtDNA.

We have provided a mitochondrial genetic diagnostic service for 25 years, testing over 10,000 probands and making a genetic diagnosis in approximately 700. The service has developed from testing a handful of common mtDNA mutations in the pre-sequencing era to whole mtDNA next generation sequencing and exome sequencing. The establishment of NHS Highly Specialised Services for rare mitochondrial disorders in the UK in 2007, with collaboration between centres in Oxford, London and Newcastle, has been key to service development.

MtDNA maintenance disorders and pyruvate dehydrogenase (PDH) deficiency are particular areas of expertise; rare and novel findings include a case of germline mosaicism for SLC25A4 associated mtDNA depletion syndrome, and several cases of mosaicism in PDHA1 associated PDH deficiency.

Finally, genetic diagnosis is critical to determining and enabling reproductive options for families, and these options now include mitochondrial donation.

Speakers' Abstracts

Session 2

Newborn Screening in Northern Ireland – where are we now and where are we headed to?

Routine screening for Phenylketonuria (PKU) in the neonatal population was started in Northern Ireland in 1960. This involved health visitors pressing a 'Phenistix' reagent strip impregnated with ferric chloride between the folds of a wet nappy. Since then the pace of change and programme expansion has been dictated in part by method development, with introduction of tandem mass spectrometry creating the potential to screen for a broader range of conditions. Programme remit has been counterbalanced through the oversight of the UK National Screening Committee (UK NSC), utilising relevant literature, pilot studies, and economic evaluation to inform recommendations on the diseases included in the newborn blood spot screening programme.

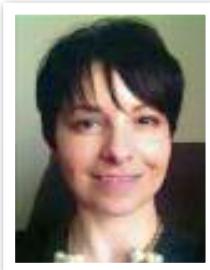
These opposing drivers have determined our current screening panel including: Phenylketonuria (PKU), Homocystinuria (HCU), Congenital Hypothyroidism (CHT), Cystic Fibrosis (CF), Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCADD), and Sickle Cell/Thalassaemia (SCT).

In an echo of the effect of tandem mass spectrometry (MS/MS) on population screening in the 1990s and early 2000s, falling costs and turnaround times for whole exome and whole genome sequencing could exponentially increase the number of prospective target conditions. However, equating the potential to employ such an approach to population screening with endorsing its implementation may lead to the opening of a Pandora's Box of ethical and interpretative difficulties.

Furthermore, advances in high resolution MS analytics and associated technologies create the possibility for application of untargeted metabolomics in screening and in provision of additional diagnostic information when paired with alternative methods.

Dr Jennifer Cundick

**Consultant Clinical Scientist,
Belfast Healthcare Trust**



BIOGRAPHY

Dr Jennifer Cundick attained her BSc(Hons: first class) and PhD in Biochemistry from Queens University Belfast. Following this, she started her training as a Clinical Scientist in Belfast Healthcare Trust. Her career to date has included positions in both the Regional Endocrine and Metabolic Biochemistry Laboratories, a sojourn in Blood Transfusion Quality, and her current role as Consultant in Newborn Screening.



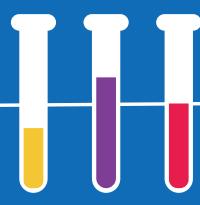
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3. Mueller C et al. Multicenter evaluation of a 0-hour/1-hour algorithm in the diagnosis of myocardial infarction with high-sensitivity cardiac troponin T. Annual emergency medicine (2016); 68(1):76-87.

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Speakers' Abstracts

Session 3



Chair:
Dr. Graham Lee

Prof. David Cowan
Director, Drug Control Centre,
King's College London

Use, misuse and abuse of steroids in sport

Dr. Conor Deasy
Consultant in Emergency Medicine
Cork University Hospital

Toxicology in the Emergency Department

Kylemore Abbey, Co. Galway

Dr. Loretta Ford
Consultant Clinical Biochemist,
Birmingham City Hospital

Biochemical investigation of legal highs



Speakers' Abstracts

Prof. David Cowan

**Director, Drug Control Centre,
King's College London**



BIOGRAPHY

Professor David Cowan is the Director of the internationally renowned King's College London Drug Control Centre which he co-founded in 1978 and which has been in the forefront of introducing advances in

anti-doping science for many years. The Centre successfully delivered the analysis of the samples collected for the comprehensive drug testing of the athletes taking part in the London 2012 Olympic and Paralympic Games at which the new biomarker test for the use of human growth hormone resulted in the disqualification of two athletes. The Centre also provided the anti-doping analysis for the Glasgow 2014 Commonwealth Games and more recently the Rugby World Cup 2015. Professor Cowan was a member of the IOC Medical Commission Games Group and Task Force for the Rio 2016 Games; a role he has also been invited to take up for the PyeongChang 2018 Winter Games.

The Drug Control Centre is based in the Faculty of Life Sciences and Medicine at King's College London. It is the only WADA accredited laboratory in the UK and one of just 32 world-wide.

Professor Cowan holds a personal Chair in Pharmaceutical Toxicology and is a Fellow of King's College London. He was awarded the International Olympic Committee Trophy for Ethics in Sport in 1998 and was one of the founder members and the first president of the World Association of Anti-Doping Scientists (WAADS). He is a Fellow of the Royal Pharmaceutical Society and was awarded Pharmaceutical Scientist of the Year in 2013. In the same year he was also awarded the Media Personality of the year by King's College London and was runner up in the Excellence in Innovation and Impact category.

His work includes bioanalysis of forensic relevance and has given evidence in both criminal (including murder) and civil cases. He has published extensively in the field of pharmaceutical analysis especially in relation to the detection and quantification of drugs and their metabolites in complex body fluids and detecting drug administration in sport. He has a particular interest in presenting science to the non-scientist, from teenagers to senior barristers and judges.

Professor Cowan was recognized in the New Years Honours List in January 2016 in which he was awarded an OBE for his services to anti-doping science.

Session 3

Use, misuse and abuse of steroids in sport

Anabolic steroids, or more correctly anabolic androgenic steroids, have been controlled in human sport since the 1970s. Initially radio-immunoassays were employed and this was changed to GC-MS methods at the Los Angeles Olympic Games in 1984. High resolution GC-MS was used at the Atlanta Olympic Games in 1996 for the first time to screen with very high sensitivity for a series of five anabolic agents. More recently, GC-tandem MS has become the main instrumental method of analysis together with LC-HRMS for some AAS. This has given us a very good means of detecting steroid misuse.

This presentation will illustrate the extent of this area of drug misuse, the source of illicit material and the harm that the abuser may suffer. It will also touch on the area of selective androgen receptor modulators (SARMs) the next generation of anabolic agents open to abuse.

Speakers' Abstracts

Session 3

Toxicology in the Emergency Department

In this talk toxicological clinical presentations and management of common toxicological emergencies will be described. The talk will describe the toxicodromes and tests used by clinicians to give clues at the bed side as to what the patient may have ingested. Drug screening will be discussed and the nuances around its use described.

Dr. Conor Deasy

**Consultant in Emergency Medicine
Cork University Hospital**



BIOGRAPHY

Conor Deasy is a Consultant in Emergency Medicine working at Cork University Hospital, Deputy Medical Director of the National Ambulance Service, Senior

Lecturer in Emergency Medicine at University College Cork and Associate Adjunct Professor at the School of Primary Care, Monash University, Australia. He is Clinical Lead for NOCA's Major Trauma Audit in Ireland, Chair of the Scientific Committee of the Irish Association for Emergency Medicine (IAEM), a member of the Irish Committee for Emergency Medicine Training (ICEMT) and an examiner for the College of Emergency Medicine.

Conor completed his higher specialist training program in Emergency Medicine in Ireland before moving to Australia where he worked as a Consultant in Emergency Medicine at the Alfred Emergency and Trauma Centre, Melbourne. While there he completed a PhD at the Department of Epidemiology and Preventive Medicine, Monash University in collaboration with Ambulance Victoria. To date Conor has published across the domains of patient safety, quality of care, systems of care, procedural sedation as well as out of hospital cardiac arrest. Conor has a particular interest in creating safe, robust, lean patient care pathways in the emergent and acute care settings.

Qualifications

MB, BAO, BCH, BMedSc, DCH, DIMC, Dip Tox, MRCSA&E Ed, FCEM, FACEM, PhD.

Speakers' Abstracts

Session 3

Dr. Loretta Ford

**Consultant Clinical Biochemist,
Birmingham City Hospital**



BIOGRAPHY

Dr Loretta Ford has been a Consultant Clinical Scientist worked at City Biochemistry Department for over ten years. Since completing her training Loretta has

worked at SWBH NHS Trust in Birmingham helping in the development of specialist testing services. In 2010 Loretta moved to the clinical toxicology laboratory where she is now the Consultant leading this national service.

Biochemical investigation of legal highs

The last 10 years has seen a dramatic change in drug use with the rise in popularity of so called legal highs, new psychoactive substances NPS. Screening for NPS represents a particular challenge as they are not detected by traditional techniques such as immunoassay.

In 2013 we introduced the first UK clinical service for routinely screening unknown drugs in patients using a Waters Xevo G2 QToF (time of flight, TOF) detector which NPS. Here we demonstrate the advantage of this technique over a traditional toxicology screening service, especially for aiding clinicians in accurate diagnosis and management in real time.

Speakers' Abstracts

Session 4



Chair: Dr. Damian Griffin

Dr. Margot Bolster, Assistant State Pathologist

The three-legged stool – The role of Toxicology in the Coroner's Autopsy

Clinical Translational Research Hotspot

Dr. Matthew Johnson, University of Exeter

Insights into beta-cell autoimmunity from monogenic diabetes

Dr. Haley Ellis, UCD and Sloan Kettering Memorial, NY

Biomarkers of Targeted Therapy Resistance in Breast Cancer

Did you know? Session Moderator: Ms. Caroline Joyce

*Dunguaire Castle,
Kinvarra, Co. Galway*

Quirky enzyme myths and truths

Micheál Ryan

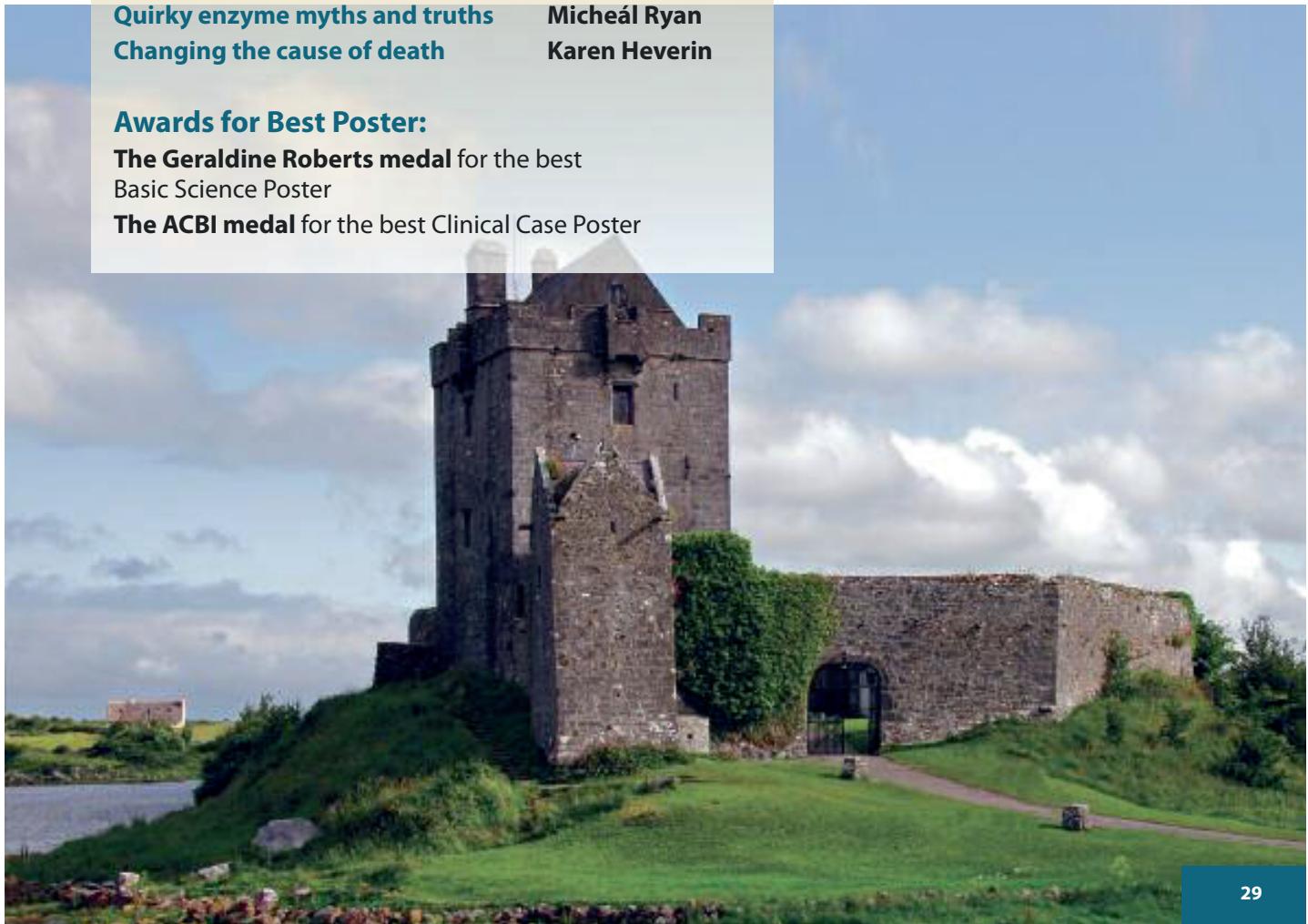
Changing the cause of death

Karen Heverin

Awards for Best Poster:

The Geraldine Roberts medal for the best Basic Science Poster

The ACBI medal for the best Clinical Case Poster



Speakers' Abstracts

Session 4

Dr. Margot Bolster

FRC Path, MB, BCh

Assistant State Pathologist &

Forensic Pathologist

Cork University Hospital



BIOGRAPHY

Dr Margot Bolster is a medical graduate of Trinity College Dublin. She trained in Cork and acquired specialist forensic pathology training in Edinburgh. She provides assistance to

the State Pathologist on a part-time basis dealing with cases typically in the south of the country.

She is Forensic Pathologist at Cork University Hospital and lectures in Forensic Medicine at University College Cork.

Speakers' Abstracts

Session 4

Insights into beta-cell autoimmunity from monogenic diabetes

Neonatal diabetes is diagnosed before 6 months of age and is generally caused by a mutation in a single gene. Traditionally it has been considered as a separate entity from the more common type 1 diabetes, which is generally diagnosed after 6 months and is caused by a combination of genetic predisposition and environmental triggers. Last generation genetic approaches have allowed great advances in the knowledge of the genetic basis of both type 1 and neonatal diabetes, challenging the conventional view of neonatal diabetes and type 1 diabetes as two completely distinct diseases.

Mutations in 24 genes have been identified to date to cause neonatal diabetes, providing a genetic diagnosis for >82% of patients diagnosed before 6 months of age. The majority of these genes are involved in insulin sensing/secretion and beta cell function/development. A notable exception are mutations in three genes (FOXP3, STAT3, and IL2RA) which cause neonatal diabetes with additional autoimmune features. These three genes are not directly involved in beta cell development or function, in fact they encode for proteins that are important for regulation of the immune system and prevention of autoimmunity. Patients with mutations in these genes have diabetes soon after birth as a result of early autoimmune destruction of their beta cells. Furthermore, these patients generally have low birth weight, suggesting that the autoimmune reaction starts in utero. These patients generally develop additional autoimmune features early in infancy and allogenic stem cell transplantation is currently the only curative therapy. The Exeter team has been specifically looking for the genetic causes of early onset diabetes and autoimmunity and has currently identified 2 further genes causing neonatal diabetes through immune dysregulation.

Uncovering the genetic basis of neonatal and type 1 diabetes broadens our understanding of the mechanisms involved in the pathogenesis of both diseases. Emerging evidence points towards a continuum model for different diabetes subtypes: from monogenic to more common forms of diabetes.

Through our integration with the diagnostic NHS laboratory in Exeter our research findings are rapidly translated into clinical diagnostics and we are able to test all known and putative genes in a single reaction. This has facilitated early diagnoses, which can have important treatment implications as many patients with monogenic autoimmunity can have targeted therapies. Furthermore, knowledge of the underlying genetic cause can enable pre-natal diagnosis, informs families and clinicians on recurrence risk and can inform on prognosis.

Dr. Matthew Johnson
University of Exeter



BIOGRAPHY

Dr Matthew Johnson is a molecular geneticist working as part of the diabetes team at the Exeter Medical School. He graduated with a BSc in Biological Science from the University of Birmingham and began his career in genetics as a technologist in the diagnostic genetics laboratory in Exeter shortly after. During his work with the diagnostic team he developed a keen interest in research, particularly in early-onset diabetes. He began a Wellcome Trust funded PhD supervised by Andrew Hattersley, Sarah Flanagan and Sian Ellard in 2014.

His research focusses on using whole genome sequencing and other next generation sequencing approaches to identify novel causes of diabetes and autoimmune disease.

Speakers' Abstracts

Dr. Haley Ellis
UCD and Sloan Kettering Memorial, NY



BIOGRAPHY

Prior to starting medicine at UCD, Haley's research at Massachusetts General Hospital and Memorial Sloan Kettering focused on molecular mechanisms of resistance to cancer targeted therapies, particularly in breast cancer. This work was published in several journals, including Cancer Cell, Nature, and Science Translational Medicine, and led to successful clinical trials.

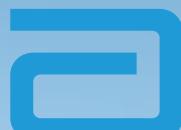
She will begin internal medicine residency training in the US next year, with plans to become a physician-scientist in the field of oncology.

Session 4

Biomarkers of Targeted Therapy Resistance in Breast Cancer

The PI3K/AKT/mTOR pathway is an established oncogenic driver in humans. Targeted biologic agents against components of this pathway have shown promising activity; however, the duration and quality of benefit remains suboptimal in unselected patients.

Improved understanding of the biologic consequence of altered PI3K/AKT/mTOR signalling is informing the development of protein and genetic biomarkers to identify patients most likely to benefit from this therapeutic strategy.

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Moored in Claddagh



Poster Abstracts

Abstract 01

Reconciling measures of glycaemic control generated by new glucose sensor-based technologies with laboratory HbA1c results

Edward (Ned) Barrett

Retired Consultant Clinical Biochemist;
E-mail: drnedbarrett@eircom.net

INTRODUCTION

The 2008 International Consensus Statement on the Worldwide Standardisation of Haemoglobin A1c Measurement included approval of HbA1c-derived average glucose calculated from the HbA1c result and reported as an interpretation of the HbA1c result.

OBJECTIVE

This study was prompted by a user of the FreeStyle Libre Glucose Monitoring System (Abbott Diabetes Care) reporting that the calculated HbA1c generated by the system was lower than the HbA1c reported by the laboratory. It set out to devise a more appropriate strategy to that dependent on average glucose concentration.

Data downloaded from the user's FreeStyle Libre reader included all sensor-generated readings of interstitial fluid (IF) glucose (a reading recorded every 15 minutes), additional IF glucose readings made by the user scanning the sensor (12 to 15 scans per day) and all blood glucose results from the reader.

RESULTS

Glycation of haemoglobin is largely determined by two key variables – glucose concentration and the time interval during which that concentration existed. The FreeStyle Libre system records both of these. Together they can be expressed as mmol/L/hour and this is used in this report as a measure of Glycaemic Impact.

While the mean sensor IF glucose concentration for this patient is 7.1 mmol/L over 90 days (8478 IF glucose readings), the median Glycaemic Impact occurs at a sensor glucose reading of 8.0 mmol/L. Using the lever as an analogy, the sensor glucose reading of 8.0 mmol/L at which median Glycaemic Impact occurs in this patient can be regarded as the fulcrum and it relates more closely to the laboratory HbA1c than the average sensor IF glucose value.

CONCLUSION

The Glycaemic Impact concept as described and used in this report is a scientifically valid alternative to calculations based on average glucose and its calculation should be included in the application software of glucose sensor-based technologies.

Abstract 02

The clinical utility of Growth Differentiation Factor-15 (GDF-15) in patients diagnosed with Diabetic Kidney Disease (DKD).

Hamon* SM¹, Griffin* TP^{2,3}, Islam MN^{1,3}, Griffin MD^{3,4}, O'Shea PM¹

¹ Department of Clinical Biochemistry, Galway University Hospitals (GUH), Galway, Ireland.

² Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals (GUH), Galway, Ireland.

³ Regenerative Medicine Institute at CÚRAM SFI Research Centre, School of Medicine, National University of Ireland Galway (NUIG), Galway, Ireland.

⁴ Department of Nephrology, Galway University Hospitals (GUH), Galway, Ireland.

*Contributed equally to this work.

INTRODUCTION

Diabetic kidney disease (DKD) accounts for 38% of patients with end-stage renal disease. Growth differentiation factor-15 (GDF-15), a stress responsive cytokine, is a promising early marker of DKD.

AIM

This study aimed to establish normative data and evaluate the clinical utility of GDF-15 in DKD using the Roche Diagnostics electrochemiluminescence immunoassay (ECLIA) in an Irish population.

METHOD

Following informed consent, 155 healthy Irish Caucasian subjects and 126 patients with diabetes, 79 with and 47 without DKD were recruited. Participants were required to attend a site visit to have blood (20 ml) collected for biochemical/haematological analyses, urine for albumin:creatinine ratio (ACR), blood pressure and patient demographics (age, gender and ethnicity) recorded. Reference intervals were determined using the 2.5th and 97.5th percentiles for GDF-15. Clinical utility was assessed using Receiver Operator Characteristic (ROC) curve analysis.

RESULTS

Of 155 healthy participants, 40 failed to meet the study inclusion criteria. The reference interval for serum GDF-15 was 275ng/L (90% CI: 254-297)-1138ng/L (90% CI: 999-1281). The area under the ROC curve was 0.935 (95% CI: 0.898-0.963; P<0.0001). The optimum GDF-15 cut-off for predicting DKD was >1270ng/L providing a diagnostic sensitivity and specificity of 91% and 85% respectively and positive likelihood ratio of 5.9:1.

CONCLUSION

The reference interval for GDF-15 in a healthy Irish population using the Roche Diagnostics ECLIA was established and the potential of GDF-15 as a screening test for DKD determined. Further prospective validation with a larger DKD cohort is required before the cut-off presented here could be recommended for clinical use.

Poster Abstracts

Abstract 03

Iron indices as markers for iron overload

O'Brien A, Kelleher A, Kerr B, Costello S and Joyce C
Clinical Biochemistry Laboratory, Cork University Hospital

INTRODUCTION

Hereditary Haemochromatosis (HH) is an autosomal recessive disorder of iron metabolism caused by mutations in the *HFE* gene, most notably the C282Y single amino acid substitution. The HH investigation protocol in Cork University Hospital requires a fasting transferrin saturation (%TS) greater than 45% to indicate genetic testing. The %TS is a calculation derived from serum iron and transferrin (TF) concentration. Serum iron is subject to diurnal variation and TF is a negative acute phase protein (APP), therefore both variables will affect %TS calculation. Conversely, Ferritin is a positive APP which is non-specifically elevated in a range of clinical conditions. Ferritin is also used to select patients for *HFE* genotype analysis.

AIM:

To look at %TS as an index of iron overload in cases with low TF and check if %TS can be used as an index of iron overload in these cases. We will also review the associated HH genotype.

METHODS:

A search of the laboratory information system (LIMS) using Cognos software was performed over an 18 month period to extract cases with %TS greater than 45% and TF less than 1.7g/L. Laboratory results gathered for this cohort included; iron, TF, %TS, Ferritin, liver function tests and C-reactive protein. Results were further subdivided by genotype and reason for referral. Patients referred for predictive HH genotype analysis i.e. with evidence of first degree family history, were removed from the study.

RESULTS:

477 patients were identified with %TS greater than 45% and TF less than 1.7g/L, of which 90 (18.9%) were *HFE* genotyped. 67% of the subgroup with high %TS and low TF were homozygous for the C282Y mutation.

CONCLUSION:

This study indicates that despite the dietary and biological variables affecting the %TS calculation, it remains a sensitive and specific marker for Haemochromatosis.

Abstract 04

A case report of paraganglioma and papillary thyroid carcinoma in a patient with a SDHB germline mutation

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INTRODUCTION

Individuals with succinate dehydrogenase subunit B (SDHB) germline mutations are predisposed to a high incidence and malignant potential of paragangliomas. In addition, SDHB mutations have been suggested to be associated with other tumours including papillary thyroid cancer (PTC). Increased production of the new biomarker 3 methoxytyramine (3MT) is associated with metastasis of these extra adrenal tumours.

CASE PRESENTATION

Following investigations for abdominal bloating, a 57 year old female presented with an incidental finding on CT of a solid lobulated mass wrapped around the abdominal aorta. There was no history of hypertension however the patient reported intermittent palpitations, night sweats and headaches. Plasma metanephhrines were consistent with a paraganglioma. 3MT analysis was not routinely available at the time. MIBG imaging indicated no avid metastatic disease. Histology after surgical removal confirmed a diagnosis of a paraganglioma with a low mitotic index.

MANAGEMENT AND OUTCOME

Plasma normetanephrine was grossly elevated at the 3 monthly post-op review. MIBG imaging was suggestive of avid disease at 3 sites including her left forearm. The patient noted a soft tissue mass on her left forearm for approximately 25 years and experienced symptoms when it was pressed. Histology after surgical removal of this mass confirmed a paraganglioma. However, the additional abdominal and adrenal sites were inoperable. After a successful chemotherapy course, plasma metanephhrines which now included 3MT analysis were within the reference interval.

Genetic analysis revealed a SDHB germline mutation (c540G>A).

The patient underwent a total thyroidectomy after a restaging PET-CT identified a PTC. Genetic analysis of DNA extracted from the PTC did not identify loss of heterozygosity. This was further confirmed by immunohistochemistry showing preservation of the SDHB protein in the tumour. This indicates that the SDHB germline mutation was not involved in the pathogenesis of the PTC.

DISCUSSION

This case illustrates the recent biochemical and genetic advances in the management of paragangliomas. In addition, this case has added to the evidence base that certain SDHB germline mutations may not be associated with PTC.

Poster Abstracts

Abstract 05

A pilot study of Vitamin D Receptor Taql and Apal Gene polymorphisms in asthma.

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BACKGROUND

Asthma and Vitamin D deficiency are prevalent in Ireland. Vitamin D receptor (VDR) polymorphisms have been linked with asthma and with asthma risk factors such as obesity and allergy. We examined 2 VDR polymorphisms in Irish asthmatics.

MATERIALS AND METHODS

VDR Taql gene variant in exon 9 (T/C) (rs731236) and Apal (rs7975232) in intron 8 (C/T) were determined using TaqMan® Assays. Lung function, full blood count (FBC), biomarkers of allergy and systemic inflammation were all measured. Serum 25-hydroxyvitamin D (25OHD), parathyroid hormone, total calcium, alkaline phosphatases, phosphate, total IgE and CRP were analysed on the Abbott Architect ci8200. FBC was measured on the Sysmex XE-2100D. The IL-10 was determined by human ELISA.

The software used for the statistical analysis was GraphPad Prism 5, Version 5.01.

RESULTS

14 adult asthmatics (9 atopic) and 56 (6 atopic) healthy volunteers were studied. We discovered that the distribution of C and T alleles for Taql and Apal polymorphisms and genotype frequencies varied considerably between asthmatics and controls ($p<0.05$).

CT haplotype was significantly associated with asthma risk (OR 9.38 (95 % CI: 2.39 - 36.86), $p = 0.002$). Asthmatics with only TC genotype for both polymorphisms had substantially lower FEV1% compared to controls ($p<0.05$). There were no significant differences between genotypes for 25OHD level, BMI, or other biomarkers, with the exception of IgE. Patients with TC+CC genotypes for Apal had significantly lower IgE level ($p<0.05$).

CONCLUSION

Our research indicates that Taql and Apal polymorphisms are more common in asthmatics. It is possible that the Apal polymorphism is associated with the atopic asthma phenotype. More in depth investigations are necessary to explore the significance of these polymorphisms in asthma in Ireland, and also mechanisms by which they may impact the development and course of the disease.

Abstract 06

Clinical Audit: Utility of Thyroglobulin Assays in Monitoring Differentiated Thyroid Carcinoma

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INTRODUCTION

Thyroglobulin (Tg) measurements are universally recommended as part of routine follow-up examination of patients with differentiated thyroid carcinoma (DTC). Immunometric assays (IA) and radioimmunoassays (RIA) are the most common methods in use in clinical laboratories. Tg assays are subject to interference from endogenous thyroglobulin antibodies (TgAb) in certain patients. Also, first generation Tg IA's with inadequate functional sensitivities may also fail to detect early tumour recurrence.

OBJECTIVES

The aim of this study was to investigate the clinical utility of a first generation Tg IA (Siemens Immulite®) and a Tg RIA assay in monitoring DTC patients over a 4-year period from 2011 to 2015.

METHODS

Clinical and radiological evidence of disease recurrence were compared with biochemical findings in 76 DTC patients. Ethical approval for this study was granted by the Mater Misericordiae University Hospital Research Ethics Committee.

RESULTS

There was good agreement between the disease status of the patients and Tg analyses in 90% of the patients. Also, there was concordance between the Tg assays in the majority of patients who were TgAb+ (n=22). However, four TgAb+ patients were found to demonstrate evidence of Tg assay discordance. In addition, there was clinical and radiological evidence of disease recurrence prior to detectable biochemical evidence in two patients.

CONCLUSIONS

This audit demonstrates good utility for Tg assays in the monitoring of DTC, however some limitations were observed. TgAb interference with Tg assays remains an issue for certain patients in the monitoring of DTC. This audit also highlights that second generation Tg assays such the Roche Cobas Tg assay are required for improved management of these patients. A multi-disciplinary approach to monitoring patients with DTC should continue with careful clinical, radiological and biochemical assessment of each patient.

Poster Abstracts

Abstract 07

The Angiotensin Converting Enzyme 2 (ACE2) is a Substrate for γ -Secretase-Mediated Intramembrane Proteolysis.

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BACKGROUND

Angiotensin-converting enzyme 2 (ACE2) is the carboxypeptidase homolog of angiotensin-converting enzyme (ACE) and the main regulatory protein of the non-classical renin angiotensin system (RAS) [1]. In addition to its role in the regulation of blood pressure, ACE2 is the functional receptor for the severe acute respiratory syndrome coronavirus (SARS-CoV). Ectodomain shedding of the ACE2 extracellular domain has previously been reported as a key step in SARS-CoV infection [2]. The physiological significance of ACE2 shedding is not yet fully defined, although increased levels of soluble ACE2 have been shown to correlate with heart failure, diabetes and chronic kidney disease [1].

OBJECTIVE

To determine if ACE2 is a substrate for the γ -secretase protease, an intramembrane cleaving protease that has been extensively characterised due its role in the pathogenesis of Alzheimer's disease.

Study Design: Treatment of HEK293T cells overexpressing ACE2 and HUH-7 cells endogenously expressing ACE2 with γ -secretase inhibitors DAPT or LY-450139 and examination of its cleavage profile by immunoblotting.

RESULTS

Treatment of HEK293T cells overexpressing ACE2 with γ -secretase inhibitors DAPT or LY-450139 potentiated the accumulation of the ACE2 carboxy-terminal fragment (CTF). In addition, treatment of HEK293T cells co-expressing ACE2 and catalytically inactive presenilin 1 with DAPT or LY-450139 resulted in potentiated CTF accumulation. Similarly, treatment of HUH7 cells endogenously expressing ACE2 with DAPT or LY-450139 resulted in potentiated accumulation of the ACE2 CTF. Conclusion: In this study, we show that ACE2 is a novel substrate for Presenilin 1 (PS1)-containing γ -secretase protease complexes. We demonstrate that following tumour necrosis factor- α -converting enzyme (TACE)-mediated ectodomain shedding, ACE2 is cleaved by the γ -secretase protease.

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Abstract 08

Naproxen Interference with Plasma Bilirubin Measurement

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INTRODUCTION

Assay interference is an unfortunate but frequent occurrence in routine Biochemistry investigations. Typically a patient's clinical history and accompanying biochemical investigations can help identify a potentially inappropriate result. However, where a result fits the clinical context of a patient, it is possible to overlook the presence of assay interference. We describe a case of interference with plasma total bilirubin measurement by Naproxen (NSAID), using the Beckman Jendrassik and Grof method.

CASE PRESENTATION

A 14 year old girl presented to the emergency department following a collapse at school. It was reported that she had 2 episodes of facial twitching and right arm jerking. Both CT and EEG examinations were suggestive of encephalopathy. Blood gas analysis identified a high anion gap metabolic acidosis. Laboratory investigations indicated acute kidney injury. Initial liver function tests revealed normal transaminases with an isolated elevated plasma total bilirubin of 257µmol/L, however, on visual inspection it was noted that the sample was not icteric. Further investigation found that analysis of the same sample using a Roche platform gave a plasma total bilirubin within the normal reference range. Urinary organic acid analysis showed elevated levels of naproxen metabolites and subsequent serum toxicology investigations confirmed extremely elevated Naproxen levels.

Dasgupta et. al. 2010, reported positive interference in plasma total bilirubin measurement on both Beckman and Siemens platforms due to the presence of the Naproxen metabolite O-desmethylnaproxen.

Subsequent analysis of plasma total bilirubin concentration in our patient using the Beckman method showed decreasing levels as the concentration of Naproxen metabolites decreased, with levels returning to normal once the interfering metabolite was no longer present.

CONCLUSION

This is the first case identified in Temple Street that demonstrated the interfering effect of Naproxen metabolites on the measurement of plasma total bilirubin using the Beckman Jendrassik and Grof method.

Poster Abstracts

Abstract 09

Vitamin B12 deficiency and Paediatric Age Related Reference Ranges

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INTRODUCTION

Cobalamin (Vitamin B12) deficiencies are important and under-recognized cause of neurological symptoms in infants. The aetiology of disorders of cobalamin metabolism is varied, ranging from dietary deficiency in a breast-feeding mother to specific inborn errors of metabolism. Early manifestations in infancy are non-specific and can lead to a delayed diagnosis. Serum B12, TCII, urine methylmalonic acid (MMA) and plasma homocysteine are critical in the differential diagnosis.

BACKGROUND

We present three recent cases of infants with symptoms that prompted metabolic investigations. Each of the infants had increased MMA on urine organic acid analysis.

All three infants were breast-fed. B12 and folate status was assessed in infant and mother with discrepant interpretation of B12 levels based on reference ranges provided when compared with WHO guidelines.

STUDY DESIGN AND RESULTS

This prompted review of B12 reference ranges quoted by our laboratory and a range of paediatric and adult laboratories that refer samples to us. We used the CLSI Approved Guideline C28-A2 to validate the transference of established reference intervals using verification with 20 samples. We collected data from whole blood samples requested by GPs on healthy children and adolescents (2 days-18 years) from a multiethnic population measured on the Abbott Architect i2000 analyser and used data from the database randomly. We were able to verify published reference ranges from CALIPER Paediatric Reference Intervals Study.

CONCLUSION

Prompt identification and treatment of infantile B12 deficiency is important to prevent irreversible neurological sequelae. B12 deficiency should be considered in every infant with failure to thrive, seizures and hypotonia. We have introduced age specific reference ranges for serum B12 to improve sensitivity of detection hence greater identification of true deficiency or congenital conditions of B12 absorption/processing. Correct classification with appropriate paediatric reference ranges could avoid unnecessary further investigations and in delay management or treatment of infant.

Poster Abstracts

Abstract 10

Isovaleryl-CoA dehydrogenase deficiency, a rare but important cause of metabolic acidosis: The first Irish case.

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INTRODUCTION

Isovaleric acidemia (IVA) an organic acidemia, is an autosomal recessive inborn error of leucine metabolism caused by a deficiency of the mitochondrial enzyme isovaleryl-CoA dehydrogenase (IVD) resulting in the accumulation of isovaleryl-CoA derivatives. It can present with severe neonatal ketoacidosis leading to death, but in milder cases recurrent episodes of ketoacidosis of varying degree occur later in infancy and childhood. Early diagnosis and treatment with a protein restricted diet and supplementation with carnitine and glycine are effective in promoting normal development in severely affected individuals.

CASE PRESENTATION

We describe a 13 month old girl born full term to non-consanguineous Irish parents. There were early concerns about reflux and underwent surgery for pyloric stenosis at 9 days old. Due to ongoing vomiting and lethargy at 3 weeks she was referred for further investigations including ultrasound for possible reoccurrence of pyloric stenosis and given a diagnosis of GORD. At four months she was noted to have head lag and gross motor delay. She had three further episodes of vomiting requiring admissions and iv fluid rehydration.

On her 4th admission at 13 months with vomiting and diarrhoea concerns persisted regarding motor development, speech delay and dysmorphism. Prior to discharge investigations included urine organic acids.

RESULTS

Urine organic acid analysis showed markedly increased isovalerylglycine, 3-hydroxyisovalerate, isovalerylglutamate and isovalerylglycine compatible with IVA. Follow-up acylcarnitine analysis showed increased isovalerylcarnitine with depleted free carnitine. Venous blood gas (VBG) post hydration showed mild metabolic acidosis. Isovaleryl CoA dehydrogenase activity in cultured fibroblasts revealed 20% residual enzyme activity.

CONCLUSION

This is the first reported case of IVA in Ireland and highlights the importance of performing appropriate investigations including blood gas analysis and urine organic acid analysis in any infant or child with anion-gap metabolic acidosis to prevent unnecessary metabolic decompensation and neurological sequelae.

Poster Abstracts

Abstract 11

Identification through audit of a panacea to the age old problem of Emergency Department 1 hour turnaround time expectations

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INTRODUCTION

Improved turnaround times (TATs) are perceived to reduce Emergency Department (ED) stay, improve ED and laboratory efficiency as well as enhancing patient safety and satisfaction.

AIM

The aim of this project is to apply audit tools to the achievement of the Royal College of Pathologists' (RCPPath) key performance indicator (KPI) standard of reporting 90% of core blood tests within 1 hour (sample receipt to vet).

METHOD

Baseline data from April 2016 and post intervention were extracted from Business Objects XI (BOXI). Four Plan Do Study Act (PDSA) cycles were developed to evaluate capacity and demand. Questionnaires were used to gauge service user and laboratory staff opinion on issues that it was felt impacted on TAT of blood samples. The following corrective actions were implemented: A red form was developed to aid staff in identification of ED samples. Disease specific profiles were agreed with stakeholders with the objective of minimising ED stay. A staff member was assigned the role of runner between specimen reception and the laboratory and use of a centrifuge was trialled in specimen reception.

RESULTS

At baseline, 41% of core ED blood tests were available within 60 minutes. The 90th percentile was 77 minutes. This improved to 91% and 36 minutes for the 90th percentile after implementation of the corrective actions. Laboratory testing was shown to represent 44% of the total patient journey in ED. The average transport time for ED samples to the laboratory using the pneumatic tube system was 26.9 minutes. Use of a dedicated ED runner evidenced a major improvement in turnaround times (18-24 minutes). Automatic release of results could save a further 11.4 minutes.

CONCLUSION

The RCPPath KPI standard of reporting 90% of core blood tests within one hour is achievable but will require investment in staffing and IT infrastructure.

Abstract 12

Profiles of Different Urine Biomarkers in Diabetic Kidney Disease

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INTRODUCTION

Urine is an easily obtainable specimen from patients. Although there has been significant interest in urinary biomarkers of diabetic kidney disease (DKD) their optimal clinical applications have not yet been fully determined.

AIM

The study objectives were to:

Quantify eight candidate urine biomarkers from patients with different stages of DKD;

Determine how these biomarker concentrations correlate with renal indices in DKD.

METHODS

Urine samples were collected from 201 adults with diabetes and different stages of DKD.

Concentrations of sTNFR1, sTNFR2,-sICAM-1,-sVCAM-1,-MCP-1,-Adiponectin,-NGAL and KIM-1 were measured using enzyme-linked immunosorbent assay (ELISA) and adjusted for urine creatinine concentration. Urine samples from 168 non-diabetic volunteers were similarly analysed to determine a reference interval.

RESULTS

Creatinine adjusted urine concentrations of sTNFR1,-sTNFR2,-sVCAM-1,-Adiponectin and KIM-1 were increased progressively with DKD stages ($p<0.001$). Urine sTNFR1,-sTNFR2,-sVCAM-1-and-Adiponectin showed only moderate negative linear correlations with the estimated glomerular filtration rate (eGFR) ($r<-0.20$, $p<0.01$).

Subjects with micro- and macro-albuminuria had higher urine sTNFR1, sTNFR2, sVCAM-1, Adiponectin, KIM-1-and-NGAL concentrations than those with normo-albuminuria ($p<0.001$). Urine sTNFR1,-sTNFR2,-Adiponectin,-KIM-1-and-NGAL showed moderate positive linear correlations with uACR ($r>0.30$, $p<0.001$).

Urine sTNFR1 and sTNFR2 showed strong correlation with each other ($r>0.85$, $p<0.0001$). sVCAM-1 and Adiponectin showed moderate correlation between them and also with sTNFR1 and sTNFR2 ($r>0.55$, $p<0.001$).

CONCLUSIONS

This study found that the candidate urine biomarkers assessed, increased with DKD stage but were correlated more closely with the albumin to creatinine ratio (ACR) than with eGFR. We propose that the clinical predictive value of monitoring urine sTNFR1,-sTNFR2,-Adiponectin, KIM-1, NGAL-and-sVCAM-1 concentrations in DKD should be separately evaluated in patients with normal and abnormal albuminuria. Future larger studies are needed to evaluate the clinical predictive value of urine biomarkers individually and in combination.

Poster Abstracts

Abstract 13

Interferences in Proficiency Testing Samples

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INTRODUCTION

The NDTC Laboratory provides nationwide urinalysis and oral fluid drug testing service for the addiction services. As an integral part of our Accreditation to ISO 17025 standard, we participate in five proficiency testing schemes: LGC PT Drugs of abuse, LGC PT Ethanol, LGC PT oral fluid, Labquality/IEQAS for Drugs of abuse and Arvecon for EtG testing. All proficiency testing results reports are reviewed on receipt. Any issues with PT scheme are investigated and a summary report prepared.

OBJECTIVE

To review anomalous Proficiency Testing results which gave false positives in screening assays over a 3 year period, examine investigations and report on unusual findings.

STUDY DESIGN

The study will review all PT scheme results from 2015 – 2017 and any studies arising from these.

METHODS

22 PT scheme results were reviewed over a period of 3 years for unusual and noteworthy interferences. The instances are outlined, the investigations carried out are described and the reason for the result is discussed.

RESULTS

Over the 3 years of the study the following unusual cases were observed:

False Positive result for Cannabis in urine arising from baby wash

False positive result for Benzodiazepines and Cannabis in oral fluid arising from the addition of Triton X as a stabiliser

False positive result for Amphetamines in urine arising from Mebeverine

CONCLUSION

Some Proficiency scheme samples are adulterated at source with a view to informing laboratories. This adulteration can give rise to anomalous findings and the detailed investigations into the anomalous results of testing for these samples which are required to satisfy the demands of an accredited quality system can be very time consuming. While informative, such contrived samples can be unrealistic in relation to monitoring performance in authentic patient samples.

Poster Abstracts

Abstract 14

Immunotherapy interference in serum protein electrophoresis in patients with Multiple Myeloma

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A 52 year male was diagnosed with multiple myeloma with an IgG Lambda (IgG λ) monoclonal protein of 8.8g/L. Over the subsequent 24 months, he was monitored regularly using Capillary Zone Electrophoresis (CZE) and immunofixation (IFX). During this period the IgG λ persisted and the level rose to > 20 g/L.

Two years later he began treatment with monoclonal antibody therapy and his monoclonal IgG λ level decreased to < 2.0 g/L. However, on IFX, the band then appeared as an IgG Kappa (IgG κ) in the gamma region. A repeat sample was requested to confirm the result. This sample confirmed the previous findings. Further investigation revealed the patient was being treated with humanised IgG Kappa monoclonal antibody DARZALEX® (Daratumumab). Daratumumab has been reported as an interferant in electrophoresis and immunofixation results in patients with IgG myeloma protein (1).

The International Myeloma Working Group states that complete response criteria include the elimination of detectable M-protein in peripheral blood (2). Therefore DARZALEX® treatment has the potential to falsely indicate poor response to therapy.

This case highlights the problem in the interpretation and reporting of electrophoresis when the laboratory staff do not have details of the patient's medical history and treatment.

If known, the IFX can be performed using the Hydra shift 2/4 Daratumumab kit to eliminate this interference (3). In this case the IgG κ was no longer visible in the gamma region and IFX confirmed treatment response.

It is important that both medical and laboratory staff are aware of their interferences in CZE and IFX. As therapeutic monoclonal antibodies are now becoming more widely used, laboratories should have a strategy in place to overcome this issue.

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Poster Abstracts

Abstract 15

Evaluation of thyroglobulin antibody interference with the Roche Cobas Thyroglobulin® II assay.

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INTRODUCTION

Thyroglobulin (Tg) measurements are recommended as part of routine follow-up examination of patients with differentiated thyroid carcinoma (DTC). Tg assays including the Roche Cobas® Tg II assay are subject to interference from endogenous thyroglobulin antibodies (TgAb). This may potentially lead to the mismanagement of patients. Roche Diagnostics recommend thyroglobulin concentrations should be confirmed with their Cobas Tg II Confirmatory test or preferably verified by determining the presence of TgAb.

OBJECTIVES

The aims of this study were to assess the performance of the Roche Cobas® Anti-Tg assay and to evaluate the Roche Cobas® Tg II Confirmatory test.

METHODS

The analytical performance of the Roche Cobas® Anti-Tg assay was verified using the ACB protocol. A method comparison was performed with the Abbott Architect® Anti-Tg assay in 112 clinical samples. The Roche Cobas® Tg II Confirmatory test was performed in 104 clinical samples which included samples with confirmed TgAb interference (n=13).

RESULTS

The Roche Cobas® Anti-Tg assay was found to have an overall imprecision of $\leq 5.1\%$, limit of quantification of 12.2 IU/mL and linear up to 1261 IU/mL. There was close agreement (89%) with the Abbott Diagnostic Anti-Tg assay in the assessment of TgAb status (Chi-square = 59.05, p<0.0001). All samples including those with known TgAb interference had % Tg recovery within the recovery range quoted by Roche Diagnostics (70-130%). However, for those samples with known TgAb interference there was a statistically lower % Tg recovery (p <0.0001).

CONCLUSIONS

The Roche Cobas® Anti Tg assay was found to be a robust assay for the analysis of TgAb. The Roche Cobas® Tg II Confirmatory test however did not identify patients with TgAb interference when the quoted recovery range was used. Further work may be required to determine if an alternative cut-off for recovery may improve the utility of this test.

Abstract 16

Evaluation of a novel immunoassay for urinary Zopiclone testing

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INTRODUCTION

The NDTC Laboratory provides a nationwide urinalysis drug testing service using Immunoassay and LC/MS techniques. In 2016 the laboratory tested approx. 180,000 urine samples by Immunoassay and approx. 8000 samples by LC/MS, including almost 6400 for Zopiclone. Huge demand exists for Zopiclone testing due to widespread abuse of this prescription drug and its implication in drug deaths¹.

OBJECTIVE

A new Immunoassay from Ark, became available in a trial version in 2016. The objective was to set up and validate this Immunoassay on a Beckman Coulter AU5800 chemical analyser and to carry out a method comparison between the Immunoassay and our current LC/MS Zopiclone assay.

STUDY DESIGN

After successful set-up and calibration, a 5 day precision study was completed, followed by a method comparison of samples analysed initially for Zopiclone by LC/MS and later by Immunoassay. 211 client urine samples (Zopiclone positive and negative), were compared across the two methods.

METHODS

Evaluation was carried out based on the comparison of the qualitative result achieved by both methods. Challenges arose due to the differing preparation steps involved in the two analysis types (neat analysis 'v' dilute and shoot' testing) and the differing cut-offs (10 ng/ml 'v' 250 ng/ml) for Immunoassay and LC/MS respectively.

RESULTS

The Immunoassay showed good intra-laboratory imprecision of 4.5% and concordance of 89% (188 of 211 matches) with the LC/MS, despite the differing cut-offs and sample preparation techniques. Upon further investigation of the LC/MS chromatograms of the 23 'non-concordant' samples, Zopiclone was detectable, under the 250 ng/ml cut-off, in 21 of these samples.

CONCLUSION:

These results indicated that the Ark Zopiclone Immunoassay could be a useful tool for urinary Zopiclone screening.

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Poster Abstracts

Abstract 17

Better sample, Better result - An Oral Fluid Sample Quality Improvement Project

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INTRODUCTION

The NDTC Laboratory provides a nationwide and flexible drug testing service to meet Ireland's ever changing drug testing demands. In 2010 an external review of the Methadone Treatment Protocol in Ireland¹ recommended the implementation of oral fluid as a testing matrix. The Laboratory responded to this by introducing oral fluid testing in 2012.

We currently test approx. 1,700 oral fluid samples per annum. However, we regularly encounter issues with the compliance of the oral fluid samples in relation to our labelling requirements, and the Quantisal collection device requirements for adequate sample volume.

OBJECTIVE

To define and target the main problems observed with the oral fluid samples received in the laboratory, by means of an audit. The ultimate objective is to improve the utility of oral fluid as a drug testing matrix.

STUDY DESIGN AND METHOD

All oral fluid samples received within a 5 month period (n=301) were visually examined for the following characteristics;

1. Indicator colour i.e. Blue/Not blue?
2. Paddle present and submerged in buffer, Yes/No?
3. Sample labelling requirements met?

RESULTS

Among the 301 oral fluid samples examined, less than one third were completely compliant i.e. were fully labelled, had a blue indicator and a submerged paddle. 5% were completely non-compliant i.e. could not be analysed. Extra issues were also documented.

CONCLUSION

To address the high level of non-compliance, the laboratory designed and issued detailed instructions for the Quantisal device, accompanied by a bespoke audit summary report, to the relevant clinics, in an effort to improve the quality of the samples received.

The effect of this measure will be re-audited in the coming months.

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Abstract 18

Glucose determination at Point of Care using Blood Gas Analyser – a worthy substitute for laboratory analysis in the oral Glucose Tolerance Test

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BACKGROUND

World Health Organisation (WHO) best practice guidelines for identifying patients with diabetes/pre-diabetes advise that samples for blood glucose should be placed in ice-water prior to analysis, a recommendation seldom practiced.

OBJECTIVE

To investigate the use of POCT and correlate the results from oral Glucose Tolerance Tests (oGTT) with laboratory analysis for samples taken in fluoride oxalate with one set preserved on ice and a second set as per established routine practice (no ice).

METHODS

19 patients scheduled for oGTT in the Mater University Hospital were consented and recruited. Fasting and 2-hour glucose samples were obtained as follows; Set 1 no ice, Set 2 on ice, Set 3 analysed immediately on a POC ABL90 Flex blood gas analyser.

RESULTS

oGTT, using samples without ice, was found to have poor sensitivity for the diagnosis of diabetes mellitus (DM) (57%, 4 of 7) and for the detection of Impaired Fasting Glucose (IFG) (0%, 0 of 5) or Impaired Glucose Tolerance (IGT) (60%, 3 of 5), when compared to oGTT performed following WHO pre-analytical recommended practice.

oGTT performed utilising venous whole blood at POC for glucose analysis was 100% sensitive for both the diagnosis of DM and the detection of IGT, and 60% sensitive for the detection of IFG when compared with best practice sample handling.

68% (13 of 19) of participants who had an oGTT had abnormal fasting glucose results (>6 mmol/L) (samples on-ice) as compared to 74% (14 of 19) with analysis at POC and 37% (7 of 19) (no ice).

CONCLUSION

There is under-diagnosis of DM and misclassification of IFG and IGT when samples are not preserved on ice during oGTT. Venous whole blood analysis for glucose at POC should be considered a good alternative.

These results suggest that a change of practice to either inhibiting glycolysis through sample preservation on ice or through immediate analysis using a robust POC method is optimal.

Poster Abstracts

Abstract 19

Are we well adjusted? – A multicentre analysis of adjusted calcium.

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INTRODUCTION

Adjusted calcium (AdjCa) calculations compensate for the wide intra-individual variability in albumin (Alb) concentration. Thus, reporting of AdjCa alongside or in place of total calcium (TCa) is recommended. Although guidance on deriving local AdjCa equations is available, data are lacking on the effects of local parameters on rates of hyper- and hypo-calcaemia.

OBJECTIVES

Study objectives were to: derive and compare AdjCa equations across multiple sites and analytical platforms; observe differences in local AdjCa Reference Intervals (RIs) and their effect on designation of hyper/hypo-calcaemia; compare local RIs with UK Pathology Harmony (PathHarm) values.

STUDY DESIGN

Sites used the methodology described in the 2015 ACB position paper to derive AdjCa formulae. Data were obtained from each site specific Laboratory Information System and trimmed accordingly. Regression equations explaining the relationships between TCa and Alb (Alb, Bromocresol green (BCG) methods) were derived. Using the regression slope and intercept, the AdjCa equation was given as follows:

$$[\text{AdjCa}] = [\text{TCa}] - (\text{slope} * [\text{Alb}]) + (\text{mean}[\text{TCa}] - \text{intercept})$$

RIs for AdjCa were determined using the CLSI C28-A3 guidance (2.5–97.5th percentile).

RESULTS

Regression analysis demonstrated good agreement between sites, as evidenced by the narrow range of values for the slope (0.014–0.016) and intercept (1.65–1.70 mmol/L). The median Alb (43–45 g/L) and TCa (2.35 mmol/L) agreed across sites but differed markedly from that quoted by Payne's formula (40 g/L) and by PathHarm (2.40 mmol/L), respectively. The newly derived AdjCa upper reference limit also agreed (2.51 mmol/L) and was notably different to PathHarm (2.60 mmol/L). Using the newly derived AdjCa RIs, the number of specimens biochemically classified as hypercalcaemic increased approximately 8 fold, to 2.1% in Cork, and 3.0% in Mullingar.

CONCLUSION

This study highlights the importance of deriving local AdjCa equations and RIs, that account for methodological and population differences. Failure to do so has potential for misdiagnosis, particularly of hypercalcaemia.

Abstract 20

Patient percentile monitoring as a quality indicator for laboratory performance

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INTRODUCTION

The aim of the Empower project is to enable laboratories to assess the stability and comparability of laboratory testing using patient percentile (median) data. Participation in Empower has the potential to improve laboratory quality systems in routine laboratories.

METHODS

Following the analysis (Abbott Architect c1600 analysers, n=3) of GP samples for 22 clinical chemistry analytes, daily medians were determined using laboratory middleware. This data was then submitted to the Empower's Percentiler (medians) and Flagger (% of results below ["hypo"] or above ["hyper"] flagging limits) databases, where data was compiled and compared across participant laboratories and analytical platforms. An initial review of the Empower reports prompted an in-depth focus on creatinine, through review of data from IQC, EQA and patient results (1st-7th Sept 2016 and 1st-7th Sept 2017).

RESULTS

The Empower data showed a decrease (up to 5 µmol/l) in the median creatinine concentration from April 2017 onward, with a simultaneous increase in the "hypo"-rate. EQA data from September 2017 also showed a negative bias compared to September 2016. These findings were corroborated by LIS patient data, which showed an increase in the percentage of males and females with low creatinine (RI[M]: 65-107 µmol/L, RI[F]: 46-86 µmol/L) between such time periods; increasing in males from 10.9% (n=279, 2016) to 17.8% (n=478, 2017) and 3.4% (n=87, 2016) to 8.9% (n=250, 2017) in females. Derived eGFR estimates showed fewer patients classified as CKD stages 3A to 5 in 2017 (23%) compared to 2016 (30%).

CONCLUSIONS

Patient percentile monitoring provides continuous assessment of analytical performance, harnessing data that the lab generates routinely, sidestepping potential quality pitfalls such as non-commutability of IQC material or EQA sample instability during transit. The Empower databases are resources that can play a supportive and complementary role to IQC and EQA in laboratory quality assessment, at no extra financial cost to the laboratory.

Poster Abstracts

Abstract 21

Macroamylase – Sheep in Wolf's Clothing?

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INTRODUCTION

A raised plasma amylase in the setting of abdominal pain is always a cause for concern. In acute pancreatitis amylase levels rise and fall relatively quickly accompanied by increased urinary excretion of amylase. However, raised plasma amylase is evident in a number of other clinical situations or may be due to benign reduced clearance in the presence of macroamylase. Chronic stable hyperamylasaemia raises suspicion of macroamylase. Any of these scenarios may present with related or incidental abdominal pain. We present four cases where macroamylase was strongly suspected.

METHODS

All enzyme values U/L. Amylase RI (plasma) 28-97, (urine) 0-470. ACCR=Amylase to Creatinine Clearance Ratio: Ref: 3-5%; <1% strongly suggests macroamylase.

PEG precipitation used Macro-Prolactin procedure. PPA=Percent Precipitated Activity; RI<45%.

PATIENTS

Case 1: 36y male; 'routine' testing by GP. 12-10-16 Amy=443; phoned to GP. 18-10-16 Amy=425, UAMY=145. PPA=97.7%. Confirms macroamylase.

Case 2: 30y male; presented to GP with 'abdominal pain'. 25-7-16 Amy=275. ED admission on 12-7-16: Amy=289. Discussed with GP; recommended repeat plus urine. 6-7-17 Amy=278, UAMY=132, PPA=97.5%. Confirms macroamylase.

Case 3: 85y male; GP referral to ED with severe abdominal pain. 7-7-14 Amy=585. 9-7-14 Amy=606. 14-7-14 Amy=594; CT neg for pancreatitis, ?macroamylase. PPA=41%. 16-7-14 UAMY=614, ACCR=1.4% (using plasma 14-7-14). ACCR equivocal; overall inconsistent with macroamylase.

Case 4: 73y female; GP presentation with 'leg pain'. 31-8-17 Amy=359. Previously 10-3-17 Amy=227. Spoke to GP. 4-9-17 Amy=199, UAMY=916, PPA=45%. macroamylase very unlikely; GP to follow-up.

DISCUSSION

Acute pancreatitis is a medical emergency; in contrast, macroamylase indicates likely benign condition. Chronic hyperamylasaemia, particularly when plasma/serum amylase does not fluctuate much, should raise suspicion of macro-enzyme. However, not all such cases of persistent hyperamylasaemia are due to macroamylase. Laboratories should have appropriate protocols in place for the investigation of suspected macroamylase, including, where possible, Urine Amylase, ACCR, PEG-precipitation and/or ultra-filtration, and Lipase.

Abstract 22

Determination of calcium status: Comparison of locally derived Albumin-Adjusted Calcium with Ionised Calcium and its reliability in certain patient groups.

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INTRODUCTION

The ACB recently published a position paper on 'Albumin- adjusted calcium, in which it identified the need for studies to compare the accuracy of adjusted calcium (AdjCa) in correctly defining calcium status against the gold standard of ionised calcium (iCa) and to assess the reliability of AdjCa in critically ill, dialysis and jaundiced patients. The aim of the present study is to address these issues.

METHODS

239 samples were identified through the LIS with both an AdjCa and iCa measurement (ICU, Dialysis and jaundiced patients excluded). Additional iCa measurement was carried out in ICU (n=23), Dialysis (n= 34) and jaundiced (n=13) patients.

Methods used: Albumin, bromocresol purple (BCP); Total Calcium, 5-nitro-5'methyl-BAPTA, both on the Roche Cobas 8000; iCa, ISE on Radiometer ABL835 Flex (anaerobic sample); AdjCa = total calcium +0.012 (40 – albumin)- locally derived equation. Reference ranges: AdjCa (2.2-2.6 mmol/L); iCa (1.19 -1.35 mmol/L).

RESULTS

AdjCa compared to iCa:

(A)Routine samples

Agreement in the classification of calcium status was seen in 82% of patients. Misclassification of AdjCa (Normal) and iCa (Low) was seen in 12% of total cohort, n =28. 2/28 < 1.11 mmol/L were alkalotic. The majority of iCa results in this group were > 1.15 mmol/L (n= 19).

(B)Designated patient groups

Critically ill: 87% Agreement in calcium status. AdjCa(Normal) and iCa(Low)in remaining patients; iCa 1.14- 1.18 mmol/L.

Dialysis: 32.4% Agreement in calcium status. AdjCa (Normal) and iCa (Low) in 60%; iCa<1.15 mmol/L in 65%.

Jaundice: 77% Agreement in calcium status. ACa (Normal) and iCa (Low) in remaining patients; iCa 1.16-1.18 mmol/L.

CONCLUSION

We have verified our locally derived adjusted calcium equation by comparison to ionised calcium. Where misclassification occurred (AdjCa (Normal) and iCa (Low)), iCa levels were minimally below the reference range and unlikely to be of clinical relevance. Adjusted calcium results appear reliable in critically ill and jaundice patients but not in dialysis patients.

Poster Abstracts

Abstract 23

Familial Pseudohyperkalaemia – Case Report And Mutation Screening For The ABCB6 Variant c.2168G>A In Irish Blood Donors

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INTRODUCTION

Pseudohyperkalaemia refers to an elevated level of serum/plasma potassium (K) due to in vitro effects. Autosomal dominant familial pseudohyperkalaemia (FP) has a variable biochemical phenotype and recently the genetic basis was elucidated with mutations found in ABCB6 e.g. c.2168G>A. Moreover, while FP itself is not considered harmful to the mutation carrier per se, it has been suggested that elevated K levels in blood donated by FP patients could potentially lead to hyperkalaemia in transfusion recipients, particularly children and neonates.

OBJECTIVE

We report the biochemical investigation and genetic diagnosis of a 46 year old female patient with persistently elevated K. In addition we report the development of a TaqMan Real time-PCR for the variant c.2168G>A and the outcome of a mutation screen in an Irish cohort.

STUDY DESIGN

Serum and plasma samples from our patient were analysed for K at 37°C, 20°C and 4°C and also over a time course of baseline, 1hr, 2hr, 4hr, 6hr and 8hr. PCR and direct sequencing for ABCB6 c.2168G>A was undertaken and subsequently an assay was developed to detect wild type and heterozygote genotypes in 400 Irish blood donors.

RESULTS

Over the 8hr time course K increased in serum from baseline level of 4.8mmol/L to 11.1mmol/l, while in plasma the increase was 5.1mmol/L to 14.6mmol/L, and this was observed only at 4°C. Subsequent genetic analysis confirmed heterozygosity for c.2168G>A confirming a diagnosis of FP. An allelic discrimination assay was configured to detect the presence of c.2168G>A and this was applied to 400 blood donors to determine prevalence and allele frequency. There were no cases of FP identified amongst this cohort of 800 alleles.

CONCLUSION

FP should be considered in asymptomatic hyperkalaemia and appropriate laboratory and genetic diagnostic methods applied. The frequency of a common FP variant appears low amongst Irish blood donors although a more extensive screen should be undertaken.

Abstract 24

Indirect ISE versus Direct ISE Measurement of Serum Sodium During the Management of Profound Hyponatraemia (Na ≤ 120 mmol/L)

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INTRODUCTION

Severe hyponatraemia may be associated with significant morbidity and mortality. Recently, European and US guidelines on hyponatraemia have advocated monitoring of sodium (Na) levels, however, there is concern regarding the potential impact that differences between methods for measuring Na may have on clinical management of severe hyponatraemic states.

OBJECTIVES

This study sought to compare contemporaneous indirect and direct ion-specific electrode (ISE) measurements of Na to determine the extent of any discordance that may exist between the two methods in a cohort of patients with marked hyponatraemia

STUDY DESIGN

The LIS was searched for serum Na ≤ 120 mmol/L over a 12-month period. All episodes measured using both techniques were compared, and the difference correlated with total protein and albumin concentrations.

RESULTS

A total of 180 temporally-related indirect and direct ISE measurements were identified. Differences were calculated by subtracting the direct from the corresponding indirect ISE reading. The differences ranged from -8.7 mmol/L to 8.6 mmol/L, with a mean difference 0.32 ± 2.61 mmol/L ($p > 0.1$). However, for samples with albumin concentration 35-50 g/L, the average difference was -0.77 ± 2.58 mmol/L, while samples with low albumin concentration (≤ 34 g/L) had a difference of 1.18 ± 2.46 mmol/L, indicating discordance between the two serum albumin states ($p = 0.001$). Similarly, samples with normal total protein (66 – 87 g/L) had a difference of -1.4 ± 2.81 mmol/L, with a mean difference of 1.16 ± 2.62 mmol/L in hypoproteinaemic samples (≤ 65 g/L), again highlighting discordance between normoproteinaemic and hypoproteinaemic states ($p = 0.001$).

CONCLUSIONS

Overall, serum [Na] did not differ significantly when measured by indirect and direct ISE, however, discordance was observed in the presence of hypoalbuminaemia and/or hypoproteinaemia. Clinicians should be aware of these effects on serum Na and should ideally use one method of measurement when monitoring in severe hyponatraemia.

Poster Abstracts

Abstract 25

A Survey of Vitamin D Requesting Patterns for General Practitioners in St. James's Hospital

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INTRODUCTION

Vitamin D requests have increased dramatically in the last 5 years. In St. James's Hospital General Practitioner (GP) requests for vitamin D tripled between 2012 and 2016. The extent to which this degree of testing is evidence-based is unknown.

OBJECTIVE

This study aimed to determine the criteria used in vitamin D requesting a short survey consisting of five questions was sent to GPs in the St. James's Hospital catchment area. The questions were designed to establish the basis for vitamin D test requesting by GPs in general.

STUDY DESIGN

The survey was circulated to all GPs in the St James's Hospital catchment area. They were asked to complete it and return it to the Biochemistry Department in St James Hospital. The primary outcome was to determine if requesting and follow-up was performed using established guidelines. Returns were reviewed by the Consultant Chemical Pathologist and Principal and Senior Clinical Biochemist.

RESULTS

To date 23 Surveys have been returned. Responses showed, in many cases, a non-standardised approach to vitamin D requesting and interpretation. Reasons for requesting included bone disease (32%), ethnicity (12%), malabsorption (12%), fatigue (8%) and renal disease (4%). 12% did not indicate a specific patient group. For indications/interpretation 25% did not specify use of any specific guidelines, 38% used un-named guidelines, 19% used cut-points included with test reports and 8% used the National Osteoporosis Society (UK) and/or NICE guidelines. For additional tests 70% included bone profile followed by PTH (35%) and calcium (15%). For post supplementation follow-up the response was; none (15%), < 3 months (10%), 3-6 months (65%), 6-12 months (10%)

CONCLUSION

The survey demonstrated significant disparity of requesting patterns for GPs. The results highlight the need to provide evidence-based guidelines and specialist advice as a guide to appropriate vitamin D requesting.

Poster Abstracts

Abstract 26

HFE Genotypes in a Blood Donor Population and in Patients Tested in a Haemochromatosis Genotyping Service

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INTRODUCTION

Type 1 hereditary haemochromatosis, due to mutations in the HFE gene, has a high prevalence in Ireland. HFE genotyping is used to confirm a diagnosis of hereditary haemochromatosis, and as a predictive test in asymptomatic family members because early detection of the genetic predisposition enables prevention of irreversible tissue and organ damage.

OBJECTIVE

The aim of the study was to compare the HFE genotype frequencies in patients referred for testing to those in a control population and a previously reported Irish neonatal population.

STUDY DESIGN

HFE genotyping (C282Y and H63D mutations) was performed on samples from a cohort of 359 first-time blood donors, representing the young to middle-aged adult population. Results were compared with the genotypes of patients tested over a 15-year period in our haemochromatosis service (2,858 patients from hospital clinics and 9,720 patients referred by general practitioners).

RESULTS

The C282Y allele frequency in the blood donor population was 11.6% and the H63D allele frequency was 16.9%. These are similar to the previously-reported values determined in neonates (11% and 15% respectively). The prevalence of C282Y homozygotes among patients referred from the hospital clinics was 14%, compared to 9.4% in patients referred by general practitioners and 2.2% in the donor population. The prevalence of C282Y & H63D compound heterozygotes in these three groups was 10.5%, 11.2% and 4.2% respectively, while the prevalence of H63D homozygotes was 3.9%, 3.9% and 3.6%. The prevalence of C282Y heterozygotes in the three groups was 19.1%, 25.6% and 14.5%, and that of H63D heterozygotes was 19.3%, 19.3% and 22.8%.

CONCLUSIONS

These results show an enrichment of the disease-associated genotypes (C282Y homozygote and C282Y & H63D compound heterozygote) in the patients referred for testing from the hospital clinics and also from general practitioners, compared to the control population. This confirms a targeted selection of patients for genotyping, and the HFE genotypes of patients are not just a random selection of the population.

Poster Abstracts

Abstract 27

The Prevalence and Determinants of Vitamin D Deficiency in Older Irish Adults: Data From the Irish Longitudinal Study on Ageing

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INTRODUCTION

Few data are available examining the determinants of vitamin D status exclusively in older adults.

OBJECTIVE:

This study aimed to investigate the prevalence and determinants of vitamin D deficiency in a representative sample of the older Irish population (aged 50–98 years).

METHODS

The concentration of 25-hydroxyvitamin D (25(OH)D) was measured in 5,356 community-dwelling older Irish adults from The Irish Longitudinal Study on Ageing (TILDA). Detailed demographic, geographic, lifestyle, and socioeconomic factors were assessed by questionnaire. Proportions of deficiency prevalence were generated by season sampled. Linear regression was used to investigate the association between 25(OH)D concentration and reported risk factors.

RESULTS

The prevalence of deficiency (25(OH)D < 30 nmol/L) was 13.1% (95% CI: 12.1–14.2). Deficiency status was more prevalent in nonsupplement users, in winter, in smokers, in obese adults, the physically inactive, those living alone, and in the oldest old (>80 years). The main predictors ($p < .05$) of 25(OH)D concentration were supplement use (coefficient nmol/L: 27.2 [95% CI: 15.3–39.2]), smoking (−8.9 [−12.6–−5.2]), summer season (5.9 [2.7–9.1]), and obesity (−4.0 [−6.3–−1.7]).

CONCLUSION

Vitamin D deficiency is common among older Irish adults. These data indicate the need for targeted strategies within sections of the older population to improve vitamin D status.

Abstract 28

Vitamin D thresholds: Is the 'insufficiency' concept valid?

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INTRODUCTION

It is generally accepted that circulating vitamin D and parathyroid hormone (PTH) concentrations are inversely related. The 'ideal' vitamin concentration to prevent secondary hyperparathyroidism in the presence of low vitamin D is still debated. This is an important point in that the sequelae of hypovitaminosis D and hyperparathyroidism include increased bone pathology and fracture risk.

OBJECTIVE

The aim of this study was to identify a threshold for vitamin D concentration associated with a statistically significant and physiologically relevant elevation of PTH.

STUDY DESIGN

A gather was performed for vitamin D and PTH analysis requests by GPs in the St. James's Hospital catchment area. 1145 patients were identified. Vitamin D was analysed using mass spectrometry and PTH by a third generation assay on the Roche 8000 platform. Vitamin D concentrations were divided into subgroups with 10 nmol/l ranges (9.20 - >130 nmol/l). Mean vitamin D and PTH was calculated for each sub-group and graphed. Bonferroni correction was used to calculate significance when comparing PTH variation between the vitamin D subgroups.

RESULTS

Findings indicated a significant negative association between vitamin D and PTH concentrations at vitamin D concentrations below 30 nmol/l with an average PTH of 52 pg/ml ($p<0.0001$). Vitamin D concentrations >30 nmol/l showed no detectable association between vitamin D and PTH. For patients with vitamin D < 30 nmol/l the percentage of patients with PTH values >65 pg/ml was 50% (PTH reference range 15-65 pg/ml).

CONCLUSION

Defining vitamin D cut-offs has proven controversial. Some authorities have suggested that, given the inverse relationship between vitamin D and PTH, PTH status be used to determine a vitamin D insufficient or deficient state. In this study we demonstrate significant rises in PTH below vitamin Ds of 30 nmol/l and would suggest this as a diagnostic threshold for vitamin deficiency. We found no association between vitamin D and PTH at higher vitamin D concentrations thus questioning the validity of an 'insufficiency' state at values between 30 and 50 nmol/l.

Notes



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