

Proceedings of **ACBI 2015**
38TH Annual Conference

Association of Clinical Biochemists in Ireland

**Royal Hospital Kilmainham
Dublin**



UNESCO International Year of Light 2015

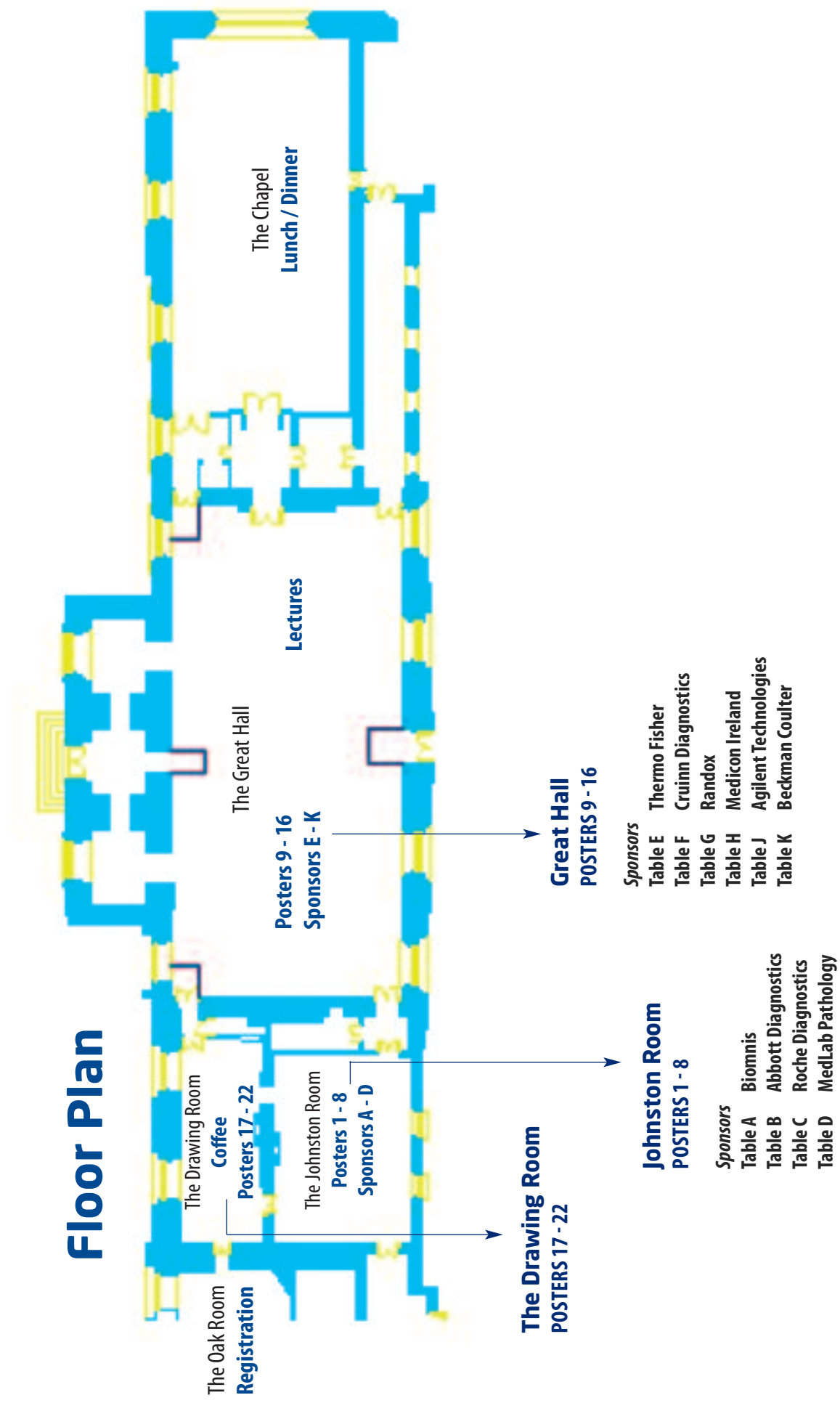
Friday & Saturday,
October 16th & 17th

2015



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Proceedings of
38TH Annual Conference
Association of Clinical Biochemists in Ireland

**Royal Hospital Kilmainham
Dublin**

October 16-17, 2015

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A message from the President of the ACBI

Once again it is a great pleasure to welcome you to the 38th Annual Conference of the Association of Clinical Biochemists in Ireland (ACBI). For 2015 we return to the magnificent surroundings of the Royal Hospital Kilmainham (RHK). We have another very interesting conference for you with sessions including Men's Health, Mother & Baby, Female Reproductive Health and Pathology and Light and Health. This year, being the International Year of Light, we have invited two speakers to talk to us on the important connection between light and health.

I encourage you to view the excellent collection of posters being displayed at the conference and I would like to thank all those who submitted their work. The Geraldine Roberts Medal will be awarded to the best scientific poster.

The RHK is the home of the Irish Museum of Modern Art and delegates will have the opportunity to visit the latest exhibitions where they will find an international display of top class artists.

Special thanks to the diagnostics industry who have continued to generously support the conference. Thanks also to the Conference Organising Committee made up of members from St. James's Hospital and the Coombe Women & Infants University Hospital and chaired by Dr. Martin Healy for their efforts in putting together such an informative and educational programme.

Finally, thank you the delegate for your participation and support of the conference. I hope you find it enjoyable and productive.

Paula O'Shea
President, ACBI



Welcome to ACBI 2015

Welcome to ACBI 2015, the 38th Annual Conference of the Association of Clinical Biochemists in Ireland. We return to the Royal Hospital Kilmainham for this year's meeting. I hope you will get an opportunity to explore some of its beautiful grounds and to visit the Irish Museum of Modern Art housed in the RHK.

Once again an excellent line-up of speakers has been assembled and because this is the International Year of Light and Light-Based Technologies we have marked the occasion with two light related health lectures.

Thanks again to all those who have taken the time and effort to submit posters. They are an interesting collection and I encourage delegates to view them over the two days.

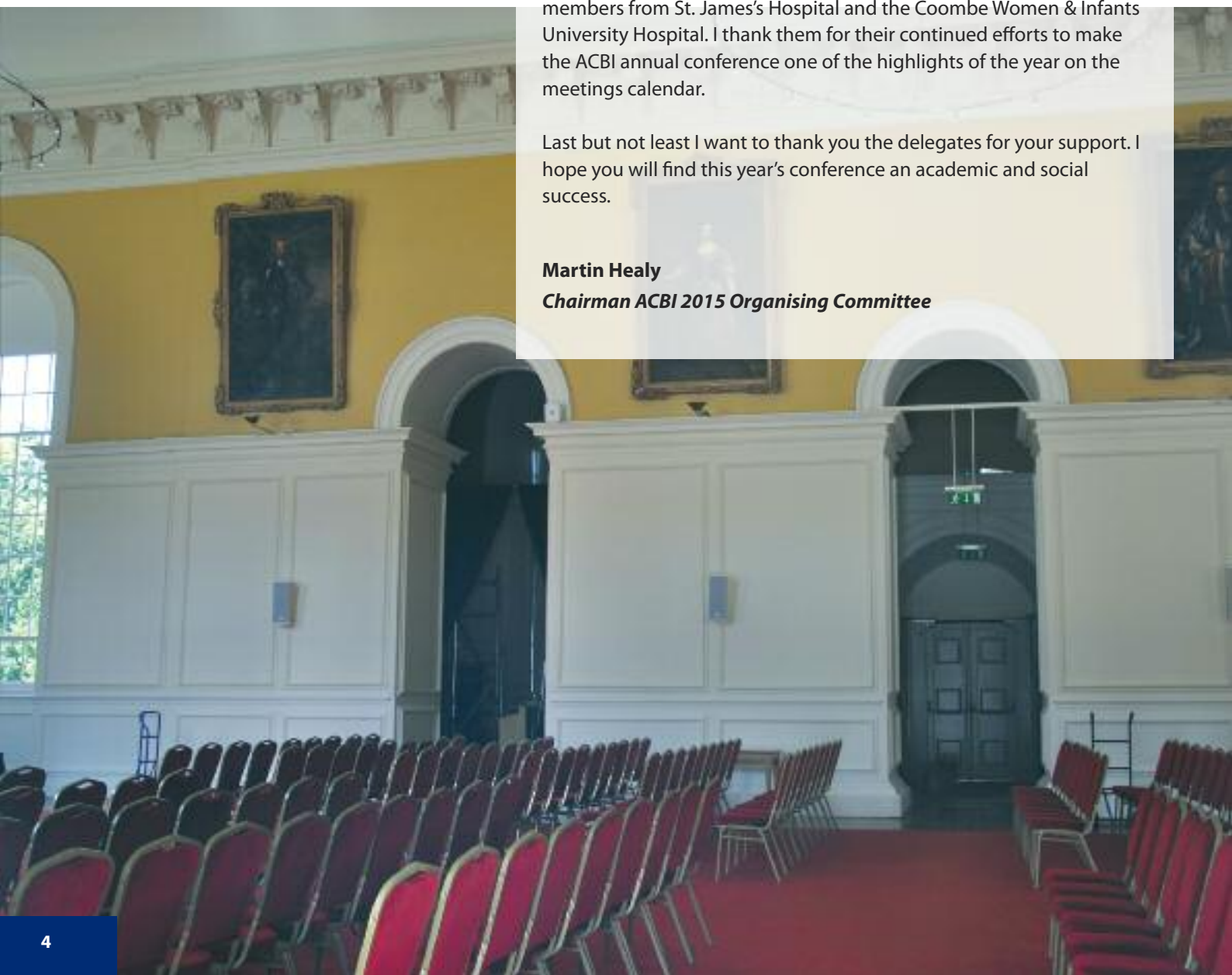
I would like to thank our corporate colleagues for their continued support of the conference. Please take time to visit them at their stands.

This year our conference committee again consisted of ACBI members from St. James's Hospital and the Coombe Women & Infants University Hospital. I thank them for their continued efforts to make the ACBI annual conference one of the highlights of the year on the meetings calendar.

Last but not least I want to thank you the delegates for your support. I hope you will find this year's conference an academic and social success.

Martin Healy

Chairman ACBI 2015 Organising Committee



Royal College of Pathologists

ACBI 2015 Conference has been approved for CPD by the Royal College of Pathologists.

7 CPD credits for the two day conference.

"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 per day and is not password protected.

For ACSLM member's to get credits log on to the ACSLM website and for:

Attendance one day: Select Continuing Education, Select 2 day conference and upload reflective learning submission.

Attending both days: Select Continuing Education, Select 2 day conference and upload reflective learning submission.

ACBI CPD Scheme

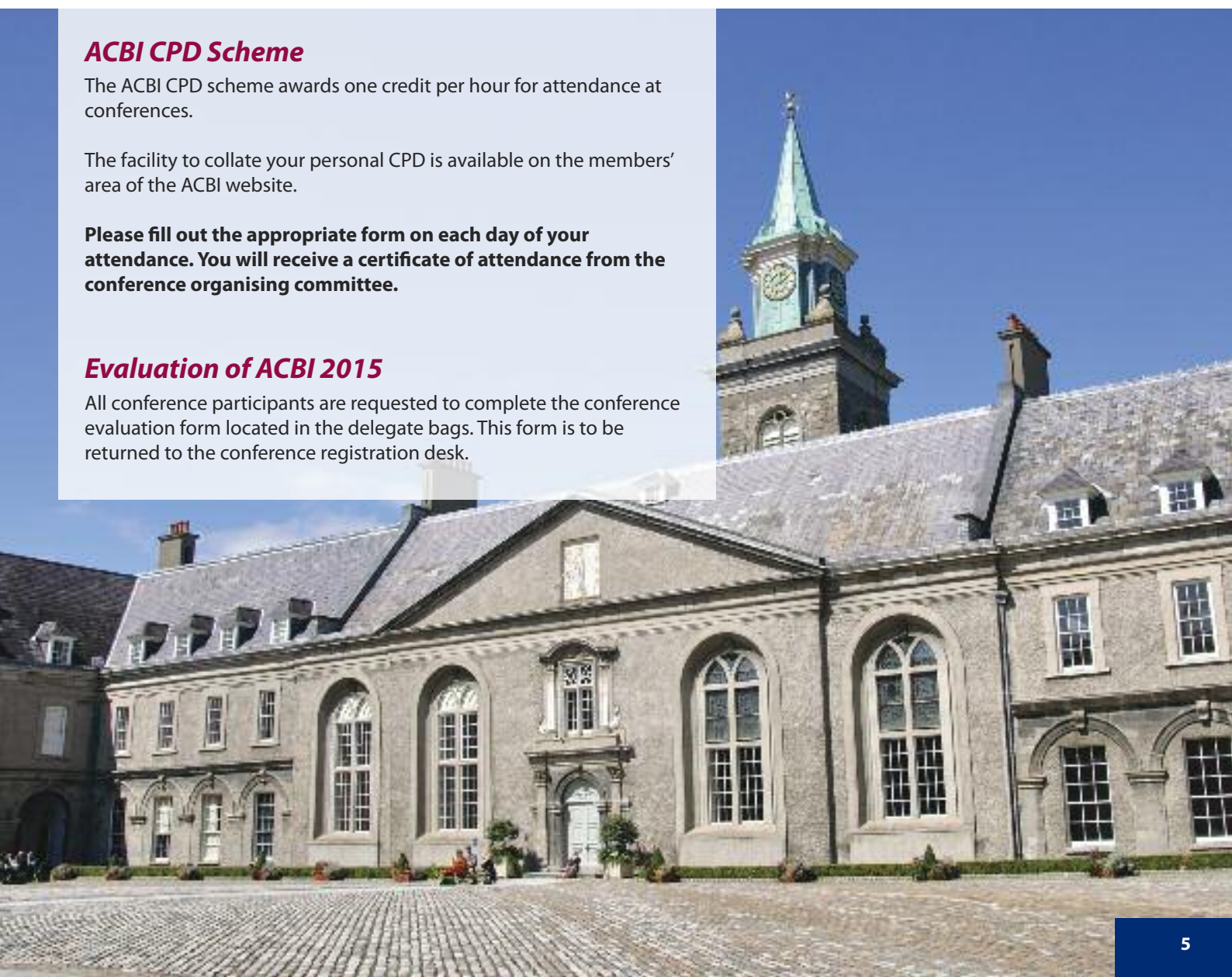
The ACBI CPD scheme awards one credit per hour for attendance at conferences.

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

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 2015

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



The Organising Committee for ACBI 2015 gratefully acknowledge the very generous support of the following:

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ACBI 2015 was jointly organised by members from

St. James's Hospital Dublin
and

The Coombe Women & Infants University Hospital
Dublin

St. James's Hospital, Dublin

Chairman: Dr. Martin Healy

Dr. Alan Balfe

Dr. Barbara MacNamara

Coombe Women & Infants University Hospital

Ruth O'Kelly

Mary Stapleton

Treasurer

Paddy Quigley



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Royal Hospital Kilmainham: Catherine O'Byrne

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Friday 16 October 2015

Conference Opening

- 08.30-10.00: Registration. Tea/Coffee/Light Refreshments
- 10.00-10.15: Conference Opening



Session 1: Friday Morning


MEN'S HEALTH

- Chair:** **Dr. Peadar McGing,**
Biochemistry Department, Matericordiae University Hospital, Dublin
- 10.15-10.55: **Professor Thomas Lynch,**
Consultant Urological Surgeon, St. James's Hospital Dublin
Men's health – We need to take a closer look at how we can improve it
- 10.55-11.15: Tea/Coffee & Poster Viewing 
- 11.15-11.55: **Dr. Fraser Gibb,**
Consultant Physician, Edinburgh Centre for Endocrinology and Diabetes,
University of Edinburgh
Androgens and type 2 diabetes
- 11.55-12.35: **Dr. Miriam Casey,**
Consultant Geriatrician, St. James's Hospital Dublin
Male osteoporosis: 'A crushing reality'
- 12.35-13.30: Buffet Lunch
- 13.30-14.00: Poster Viewing



Session 2: Friday Afternoon

MOTHER & BABY

- Chair:** **Mary Stapleton,**
Biochemistry Department, Cork University Hospital, Cork
- 14.00-14.40: **Professor Michael Turner,**
Clinical Lead HSE and Professor in Obstetrics and Gynaecology,
Coombe Women and Infants University Hospital and St. James's Hospital Dublin
The diagnosis of gestational diabetes mellitus in contemporary obstetrics
- 14.40-15.20: **Dr. Susan O'Connell,**
Consultant Paediatric Endocrinologist, Cork University Hospital
Seeing the wood for the trees – screening for neonatal hypoglycaemia – who is at risk and why do we screen?
- 15.20-15.50: Tea/Coffee & Poster Viewing 
- 15.50-16.30: **Professor Andrew Shennan,**
Professor of Obstetrics, King's College, London
Pre-eclampsia: Pathophysiology and new diagnostic markers

Friday Evening

- 16.45-17.30: ***Visit to the Irish Museum of Modern Art Exhibition
"What We Call Love – From Surrealism to Now"***
- 19.15: Drinks Reception
with music provided by Harpist Áine Ní Dhubhghaill
- 20.00: ***Annual Dinner and Musical Entertainment***
with Sean Boland

Saturday 17 October 2015

Session 3: Saturday Morning

FEMALE REPRODUCTIVE HEALTH AND PATHOLOGY

- Chair:** **Orla Maguire,**
Biochemistry Department, St. Vincent's University Hospital Dublin and the
National Maternity Hospital, Holles Street, Dublin
- 09:00-10:00: **ACBI AGM**
(Ordinary Members only)
- 10:00-10:30: Tea/Coffee/Light Refreshments/Poster Viewing
- 10:30-11:10: **Professor John O'Leary,**
Consultant Histopathologist, Coombe Women's and Infants University Hospital
and St. James's Hospital, Dublin
Ovarian cancer: Towards precision, predictive and personalised medicine
- 11:10-11:50: **Professor Richard Anderson,**
Professor of Clinical Reproductive Science, University of Edinburgh
Anti-Müllerian hormone in clinical practice
- 11:50-12:30: **Dr. John Coulter,**
Consultant Gynaecological Oncologist,
The South Infirmity Victoria University Hospital, Cork
Gestational trophoblastic disease (GTD) and establishment of a National GTD Registry
- 12:30-13:30: Buffet Lunch
- 13:30-1400: Poster Viewing and Judges Poster Tour



Session 4: Saturday Afternoon

LECTURES TO MARK THE INTERNATIONAL YEAR OF LIGHT



LIGHT AND HEALTH

- Chair:** **Dr. Derek McKillop,**
Consultant Clinical Scientist, Southern Health and Social Care Trust,
Craigavon, Northern Ireland
- 14:00-14:40: **Dr. Andrew Coogan,**
Senior Lecturer and Department Head, Maynooth University
Department of Psychology
The dark side of light-at-night
- 14:40-15:20: **Professor Antony Young,**
St. John's Institute of Dermatology, King's College London
The risks and benefits of solar UVR exposure
- 15:20-15:35: Presentation of Geraldine Roberts Medal for best scientific poster
- 15:45: Conference close

The Irish Museum of Modern Art will remain open after the conference until 5.30pm for those who wish to browse the exhibitions



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Session 1

MEN'S HEALTH

Chair:

Dr. Peadar McGing

Department of Clinical Biochemistry and Endocrinology
Mater Misericordiae University Hospital Dublin

Professor Thomas Lynch

Consultant Urological Surgeon
St. James's Hospital and Trinity College Dublin

**Mens health – We need to take a closer look at
how we can improve it**

Dr. Fraser Gibb

Consultant Physician,
Edinburgh Centre for Endocrinology and Diabetes,
University of Edinburgh

Androgens and type 2 diabetes

Dr. Miriam Casey

Consultant Geriatrician,
St. James's Hospital Dublin

Male osteoporosis: 'A crushing reality'



MedLab
PATHOLOGY

Session 1

Professor Thomas Lynch
Consultant Urological Surgeon
St. James's Hospital and
Trinity College Dublin



BIOGRAPHY

Professor Thomas H Lynch is a consultant urological surgeon at St. James's Hospital and Trinity College, Dublin. In addition to his special interest in Uro-Oncology he is the lead urologist in laboratory based

prostate cancer research with multiple publications in this area. He has been heavily involved in the development of Irish national guidelines for prostate cancer diagnosis and chaired the expert group for the Irish Department of Health.

He is involved in a number of groups for the department of health to improve the diagnosis and treatment of men with prostate cancer. He has a particular interest in the accurate diagnosis of prostate cancer and he introduced the first one stop rapid access clinic for the diagnosis of prostate cancer and these are now part of national strategy. He also has a particular interest in ways to improve mens health in general.

He has won several grant bids for research and clinical funding and several awards both for clinical and research work.

Mens health – We need to take a closer look at how we can improve it

Men always have a higher risk of injury than women due to occupational hazards and they also have higher mortality rates. In general, rate of injury at work, roads, schools and places of recreation are higher among men. Similarly, physical disabilities are higher in males. Prevalence rates of hypertension and newly diagnosed diabetes mellitus are also higher among men. This reflects the high rate of exposure to risk factors in men such as improper food intake, smoking and alcohol intake. In addition, men do not take action immediately to get treatment when they have symptoms. It is quite common for diseases to be detected late in men which increases their chance of an early death. Men feel that they should be strong or look strong in order to support the family economically and socially. This causes them not to take serious precautions to prevent disease. Men are also less prepared to attend health information talks, less likely to attend for health screening or to provide time for recreation and eating nutritious meal. Effective preventive action should be taken by the government and NGOs to promote male involvement in disease prevention activities in order to maintain the continuity of humankind in the future.

Session 1

Androgens and Type 2 diabetes

The rising prevalence of type 2 diabetes mellitus is associated with trends in obesity and ageing. Hypogonadotrophic hypogonadism is commonly encountered in diabetes, obesity and the ageing male and is labelled 'late onset hypogonadism' (LOH), as distinct from specific diseases of the hypothalamus and pituitary. It is this entity, which is responsible for the significant increase in the prescribing of testosterone replacement, observed over the past decade.

Hypogonadism is estimated to occur in up to one third of men with T2DM, although the precise definition of hypogonadism remains controversial and the underlying pathogenic mechanisms are not well understood. Even more controversial is the decision to treat such men with testosterone replacement therapy, with particular concerns raised in recent years with respect to cardiovascular safety. It is remarkable that despite such widespread prescribing, we have absolutely no high quality evidence to support the benefits of testosterone replacement in men with type 2 diabetes.

Dr. Fraser Gibb
Consultant Physician
Edinburgh Centre for Endocrinology
and Diabetes
University of Edinburgh



BIOGRAPHY

Dr Gibb graduated from the University of Edinburgh Medical School in 2000. He undertook specialist training in Endocrinology & Diabetes in Edinburgh between 2005 and 2012. He

was appointed to a Consultant post in Endocrinology & Diabetes in 2012 at the Royal Infirmary of Edinburgh. His clinical interests include the management of type 1 diabetes, inpatient diabetes care, general endocrinology and the management of differentiated thyroid cancer. Dr Gibb was awarded a PhD, from the University of Edinburgh, for research examining the metabolic effects of sex steroid hormones and has a number of active clinical research projects, particularly in the field of androgen deficiency and diabetes. He is currently Secretary-Treasurer of the Caledonian Society for Endocrinology & Diabetes

Session 1

Dr. Miriam Casey
Consultant Geriatrician
St. James's Hospital
Dublin 8



BIOGRAPHY

A consultant geriatrician in St. James's Hospital Dublin, Dr. Casey leads a large bone health and fracture prevention service. Her MD, obtained from the University of Leicester,

investigated novel biochemical markers in the assessment of bone disease, a research area that she continues to work with today.

She is a lead investigator within the The Trinity, University of Ulster and Department of Agriculture Study (TUDA) a large cross-border research project with a cohort of over 5,000 patients and is the lead investigator in the bone component of the Joint Irish Nutrigenomics Organisation Study (JINGO), a UCD led study on determination of nutritional phenotypes in the Irish population. She is also PI and grant holder on a study to examine the use of protein supplementation with pharmacological treatment in patients with severe osteoporosis.

Male Osteoporosis: 'A crushing reality'

I will be reviewing the presentation of male osteoporosis in the St. James's Hospital tertiary centre over the last 10 years and describing the clinical and laboratory approach, including specialist bone markers and DEXA, for identifying and treating this cohort.

I will identify emerging trends, associations and predictions for future occurrence of male fractures and highlight the need for future planning to manage osteoporosis in these patients.

I will outline a strategy, using fracture prediction data, for the assessment and management of male osteoporotics over the next 10 years.

Session 2

Roche

MOTHER & BABY

Chair:

Mary Stapleton

Biochemistry Department,
Cork University Hospital, Cork

Professor Michael Turner

Clinical Lead HSE and Professor in Obstetrics & Gynaecology,
Coombe Women and Infants University Hospital and
St. James's Hospital Dublin

The Diagnosis of gestational diabetes mellitus in contemporary obstetrics

Dr. Susan O'Connell

Consultant Paediatric Endocrinologist,
Cork University Hospital

Seeing the wood for the trees – screening for neonatal hypoglycaemia – who is at risk and why do we screen?

Professor Andrew Shennan

Professor of Obstetrics, King's College, London

Pre-eclampsia: Pathophysiology and new diagnostic markers

Session 2

Professor Michael Turner
Clinical Lead HSE and Professor in Obstetrics and Gynaecology Coombe Women and Infants University Hospital, St. James's Hospital and Trinity College Dublin



BIOGRAPHY

Professor Turner trained in obstetrics and gynaecology in Dublin and London, and was appointed as a consultant in 1990.

From 1992 to 1998

he served as Master of the Coombe Women and Infants University Hospital which is one of Europe's leading hospitals for women's healthcare. In 2006 he was appointed the UCD Professor of Obstetrics and Gynaecology at the Coombe. He is also Director of the UCD Centre for Human Reproduction, one of the university's dedicated research centres, which focuses on health services implementation science and on modifiable clinical risk factors for pregnancy such as maternal obesity, aberrant fetal growth, inadequate nutrition, infection and smoking. Since 2010 he has served as the country's first National Lead for the Health Services Executive Clinical Programme in Obstetrics and Gynaecology.

The Diagnosis of Gestational Diabetes Mellitus in contemporary obstetrics

Gestational Diabetes Mellitus (GDM) is a common and potentially serious pregnancy complication that has implications for the health of the woman and her offspring both short-term and long-term. While contentious, the criteria for making the diagnosis based on a screening Oral Glucose Tolerance Test (OGTT) have been made more sensitive and the diagnosis can be made based on a single abnormal reading, and not two as previously (WHO, 2013).

Our research group has examined the role of pre-analytical glycolysis of maternal plasma glucose samples in the diagnosis of GDM (Daly et al, 2015). In obese women (n=24), the diagnosis of GDM was made in 54% of women when the samples were put on iced slurry and immediately analysed, as recommended, compared with 17% when handled as usual ($p < 0.001$).

Similar results were found when we repeated the study in nonobese subjects. A national survey identified wide variations in the standards of pre-analytical handling of samples which may account for the variations in incidence previously reported between maternity units.

The current practices for the pre-analytical handling of maternal glucose samples needs to be reviewed and standards improved.

Session 2

Seeing the wood for the trees – screening for neonatal hypoglycaemia – who is at risk and why do we screen?

A brief period of hypoglycaemia (1-3 days) is commonly observed in normal newborns during transition from foetal to extra-uterine life. This is a hypoketotic form of hypoglycaemia, called transitional neonatal hypoglycaemia, which appears to be caused by a lower glucose threshold for suppression of insulin secretion than would be normal for infants, children, or adults.

This most closely resembles known genetic forms of congenital hyperinsulinism (CHI) which cause a lowering of the plasma threshold for suppression of insulin secretion.

It is speculated that the low glucose threshold for suppressing insulin release at birth reflects persistence of a foetal islet adaptation that allows the foetus to secrete sufficient insulin to maintain foetal growth even at foetal glucose concentrations that are lower than in the mother and also at times when maternal glucose concentrations are reduced.

In neonates, studies have shown that plasma insulin levels were higher and showed a larger variation in both term and preterm infants compared with older children after overnight fasting, despite lower plasma glucose levels in the neonates than in the older children. In most cases, plasma insulin concentrations are not dramatically elevated in newborns with transitional neonatal hypoglycaemia. However, this does not exclude hyperinsulinism because this lack of elevated insulin is also commonly observed in genetic forms of hyperinsulinism, which can make detection of persistent hyperinsulinism challenging.

The clinical challenge is in recognising and detecting the infant who is at risk for persistent recurrent hypoglycaemia extending beyond the expected period of transitional neonatal life. This lecture will discuss recent literature on the topic which has led to new recommendations for screening for neonatal hypoglycaemia, and the role of clinical biochemistry in diagnosis and management.

Dr. Susan O'Connell
Consultant Paediatric
Endocrinologist
Cork University Hospital, Cork

BIOGRAPHY

I qualified from UCD in 1998 and immediately commenced paediatric training. Following 2 years at National Children's Hospital, Tallaght and Trinity College Dublin I was awarded an MD in 2009 for a thesis on follow-up growth of children born small for gestational age (SGA) which also involved participation in a multi-centre clinical trial of growth hormone in children born SGA with failure of catch up growth.

Following a period as Lecturer in Paediatrics at Trinity College Dublin, I spent 3 years in a Clinical and Research Fellowship at Princess Margaret Hospital, Perth, Western Australia. I commenced my consultant post in Cork University Hospital in 2012. I am a Clinical Senior Lecturer at University College Cork. Research interests include dietary factors in management of T1DM and I currently hold a research grant from the European Society for Paediatric Endocrinology (ESPE). Other interests include severe hypoglycaemia in T1DM, imprinting and syndromic growth disorders such as Silver Russell Syndrome, Neonatal Diabetes, and disorders of sex development.

I am the Irish representative on the European Network of Human Congenital Imprinting Disorders (<http://www.imprinting-disorders.eu/>). I am the current Paediatric representative on the Committee of the Irish Endocrine Society (IES). I thoroughly enjoy my job, teaching myself and others about the wonders of Paediatric Endocrinology and am constantly on the go.

Session 2

Professor Andrew Shennan
Professor of Obstetrics
Women's Health Academic Centre
St Thomas Hospital
King's College London, UK



BIOGRAPHY

Andrew Shennan is Professor of Obstetrics at King's College London, based at St. Thomas' Hospital. He leads clinical research at the Women's Health Academic Centre, and is Deputy

Director of R and D for Guys and St. Thomas NHS Trust, which is the National Coordinating Centre for the NIHR Comprehensive Research Network.

He specialises in clinical trials in antenatal and intrapartum care. His research interests include interventions to predict and prevent preterm birth, pre-eclampsia, obstetric anaesthesia, global health and the use of blood pressure monitoring. His current research funding as applicant/co applicant is >£10m, in 15 grants. He has published more than 50 articles in the last 24 months and over 300 peer reviewed research reports in total.

He has been a member the relevant committees for the International Standardization Organization (ISO), British Standards Institute (BSI) and the British Hypertension Society (BHS). He also advises the World Health Organisation (WHO) on perinatal research and is an expert advisor to the National Institute of Clinical Excellence (NICE) Hypertension in Pregnancy CDG.

Pre-eclampsia: Pathophysiology and new diagnostic markers

Pre-eclampsia is responsible for approximately 5% of pregnancies. Hypertensive disorders of pregnancy account for >60,000 maternal deaths worldwide annually. Both maternal and neonatal morbidity and mortality are increased in pregnancies with pre-eclampsia with significant personal cost to families, and economic implications for the health service. Diagnosing pre-eclampsia is a major clinical challenge. It is characterised by hypertension and features of multiple organ disease resulting in a highly variable clinical presentation. The disease often progresses over weeks before diagnosis is confirmed. Women may present with mild late-onset hypertension, proteinuria and a normally grown baby which will have few long-term sequelae, or early-onset, severe maternal disease may be complicated by fetal intrauterine growth restriction. Even with severe disease women are often asymptomatic.

Pre-eclampsia is a disorder of abnormal placentation with subsequent maternal inflammatory and vascular response. There is an improved understanding of the underlying pathophysiology particularly relating to the role of angiogenic factors: it is established that in normal pregnancies, trophoblasts regulate spiral artery remodelling and enable normal vasculogenesis by releasing pro-angiogenic factors such as VEGF and Placental Growth Factor. Soluble Fms-like tyrosine kinase 1 (sFlt-1) is a placentally-derived variant of the vascular endothelial growth factor (VEGF) receptor, which is up-regulated in pregnancies complicated by pre-eclampsia and has been shown to antagonise VEGF and PlGF, offsetting its pro-angiogenic actions.

From first to early second trimester there are changes in sEng, PlGF and sFlt-1, and along with the addition of clinical characteristics, can predict pre-eclampsia and used to target aspirin and time surveillance from early pregnancy. Significant differences have also been demonstrated in early pregnancy of pregnancy associated para protein A (PAPP-A), a-disintegrin and metalloproteinase 12 (ADAM12), placental protein 13, angiopoietin 1 and 2, interleukin-1 beta and fibrinogen, and hCG, although this has not lead to a reliable prognostic tool for the disease.

The most likely area of clinical utility for PlGF is in 'point of care' testing in women posing a diagnostic challenge to the clinician. It could have a substantial impact on health resource use, avoiding unnecessary admissions those in who will have a more benign disease course and a longer 'time to delivery' interval, identified on the basis of a normal test. Such a test could contribute to risk stratification of women presenting with suspected pre-eclampsia – highlighting those with low PlGF to intensive surveillance to avoid adverse outcomes including fetal demise. Trials are underway to confirm this utility.

Session 3



FEMALE REPRODUCTIVE HEALTH AND PATHOLOGY

Chair:

Orla Maguire

Biochemistry Department,
St. Vincent's University Hospital Dublin and the
National Maternity Hospital, Holles Street, Dublin

Professor John O'Leary

Consultant Histopathologist, Coombe Women's and Infants
University Hospital and St. James's Hospital, Dublin

**Ovarian cancer: Towards precision, predictive
and personalised medicine**

Professor Richard Anderson

Professor of Clinical Reproductive Science,
University of Edinburgh

Anti-Müllerian hormone in clinical practice

Dr. John Coulter

Consultant Gynaecological Oncologist,
The South Infirmery Victoria University Hospital, Cork

**Gestational trophoblastic disease (GTD) and
establishment of a National GTD Registry**

Session 3

Professor John J O'Leary
Consultant Histopathologist
Coombe Women & Infants
University Hospital
and St. James's Hospital Dublin



BIOGRAPHY

I am Chair of Pathology at Trinity College Dublin [TCD], Director of Pathology at the Coombe Women and Infants University Hospital, Dublin, Consultant Pathologist at St.

James's Hospital, Dublin, Ireland and a named PI at the Biomedical Diagnostics Institute [BDI], Ireland.

I am a clinician scientist who has over 400 publications [200+ peer reviewed papers, >250 published abstracts, 29 book chapters and 3 books] with publications in Nature, Nature Medicine, Nature Immunology, The Lancet, PLoS One etc. I lead a multi-investigator unit at Trinity College Dublin [TCD], composed of 44 scientists.

I am the lead/champion for cancer research at TCD. My research group works in the following cancer areas: prostate, ovary, cervix, head and neck, cancer stem cell biology, the cancer inflammasome, metastasis and circulating tumour cells [CTCs] and pregnancy transcriptomics and proteomics. My research group has raised in excess of 55 million euros in grant income over the past 4 years and our laboratory currently hosts 4 EU 7th FP grants. I have brought 35 PhD, 7MD successfully to completion. There are currently 13 PhD students in my group and 23 post-doctoral scientists.

Ovarian Cancer: Towards precision, predictive and personalised medicine

The outcome for ovarian cancer is poor with 75% of women diagnosed late in their disease [stage II/IV], with a high risk of recurrence and chemoresistance. Currently the only markers used in ovarian cancer detection include CA-125 and CA19.9, which are not accurate screening tools.

This talk will focus on four aspects of ovarian cancer biology: a). Metastasis and the central role played by altered coagulation; b). Novel prognostic markers in ovarian cancer – MAD-2 and My D88, that exquisitely define the risk of recurrence and chemoresistance in ovarian cancer; c). Autoantibody-profiling in early and advanced ovarian cancer; d). The 'hypoxiome' of ovarian cancer as related to disease recurrence and chemoresistance risk.

We will explore some novel molecular biological mechanisms driving chemoresistance, recurrence and metastasis and will define the unique properties of ovarian cancer stem cells.

Session 3

Anti-Mullerian Hormone in Clinical Practice

Conventional hormonal analysis function has focused on the measurement of the hormones that are primarily associated with ovulation, ie the gonadotropins and sex steroids. While these are of undoubted importance for understanding that key aspect of ovarian function, the advent of measurement of anti-müllerian hormone (AMH) has allowed insight into earlier stages of development of ovarian follicles, and this has led to an explosion of interest in this biomarker, both for research and clinical care.

AMH is secreted by the ovary throughout the reproductive lifespan, with serum concentrations increasing through childhood to a peak in early adulthood and then a subsequent decline to the menopause. Its most established clinical use is in prediction of response in assisted reproduction and, indeed, is in routine use in many IVF clinics. It has potential diagnostic use in polycystic ovary syndrome (PCOS) and it is being explored as a predictor of remaining reproductive lifespan, ie time to and age at the menopause. This application is also of value in the context of oncofertility, both in predicting ovarian function after chemotherapy, and identifying women with previously-undetectable loss of the ovarian reserve following treatment.

There have been significant issues with assays over the last few years, but recently automated assays have been developed and are likely to prove more robust and reproducible, and have improved sensitivity. There remains, however, a significant gap with the absence of an international standard.

Professor Richard Anderson
Elsie Inglis Professor of Clinical Reproductive Science, University of Edinburgh
Head of Section, Obstetrics and Gynaecology, University of Edinburgh
Consultant in Reproductive Medicine, Royal Infirmary of Edinburgh



BIOGRAPHY

Training in medicine was punctuated by PhD in MRC Brain Metabolism Unit in neuroendocrinology. Subsequently trained in Obstetrics and Gynaecology in Edinburgh, including a WHO

Research Fellow post in Hormonal Male Contraception. After completing Subspecialty training in Reproductive Medicine as a lecturer at the University of Edinburgh with David Baird and a year in Sam Yen's lab in San Diego I returned to the MRC Human Reproductive Sciences Unit in 1998 with a consultant post at the Royal Infirmary of Edinburgh. Subsequently appointed to current post in the University in 2005: over subsequent years I have established a group investigating the female reproductive lifespan, with both laboratory and clinical aspects focusing on the establishment of the follicle pool in fetal life, and the assessment and mitigation of iatrogenic damage in girls and women. This includes the development of the UK's first ovarian cryopreservation service for fertility preservation.

Session 3

Dr. John Coulter
Consultant Gynaecological
Oncologist
The South Infirmery Victoria
University Hospital
Cork



BIOGRAPHY

Dr John Coulter is a practicing Consultant Gynaecological Oncologist at Cork University Maternity Hospital. A UCC graduate in 1989, he underwent general surgical training for 3 years and attained

Fellowship of the Royal College of Surgeons in Ireland (FRCSI). After general training in Obstetrics and Gynaecology from 1993 to 1998 both in Cork and The Coombe Womens and Infants University Hospital, Dublin, he travelled to Australia and completed a 3 year RANZCOG Fellowship training scheme in Gynaecological Oncology and is a certified Gynaecological Oncologist (CGO). He is currently a consultant in Cork and is chairman of the Cork Gynaecological Oncology Group Multidisciplinary Team. He is a member of the National Cancer Control Program guideline committee on hereditary gynaecological cancers and is Clinical Director of the National Trophoblastic Disease Registry and Treatment Centre.

Gestational trophoblastic disease (GTD) and the establishment of a National GTD Registry

Gestational Trophoblastic Disease (GTD) is a disease of the developing placenta that occurs due to abnormalities in the genetics of conception. Approximately 1/600 pregnancies are affected by this abnormality that results in a "molar pregnancy". Molar pregnancies are usually suspected at early pregnancy ultrasound and can result in malignant transformation of the placenta with the possibility of widespread metastatic disease requiring chemotherapy in up to 15% of cases. Based on our estimated number of babies delivered in Ireland there are approximately 150 new cases annually in this country.

Following surgical evacuation of the uterus (ERPC) as initial management of the disease, every woman requires close clinical follow-up to determine whose disease will resolve spontaneously (85%) and who will require chemotherapy. Serum levels of hCG need to be monitored on a weekly basis for every woman. This requires close interaction between the diagnosing pathologist, the treating physician and clinical biochemist on a constant basis and an understanding of the assay platforms and isoforms of hCG being measured are very important in clinical practice.

Eighty five percent of patients will have normal regression of hCG levels after surgical management and require 9 months of follow up before being allowed to achieve another pregnancy. Thus, 15% of patients will require chemotherapy to cure their trophoblastic disease based on abnormally regressing hCG levels as determined by the specialists with expertise in the management of GTD.

Unfortunately many patients with GTD in Ireland have not been managed consistently and appropriately due to the lack of a specialist integrated care. Therefore, many Irish patients in the past have had to have specialist treatment at Charing Cross Hospital in London, a world renowned centre of excellence.

As a gynaecological oncologist with a specialist interest in GTD and member of the clinical leads in gynaecological oncology at NCCP, I proposed to establish a National GTD Registry and Multidisciplinary Treatment Centre to centralise the management of all women in Ireland with trophoblastic disease. NCCP have supported this initiative. The HSE have also enthusiastically supported this integrated care initiative with funding through the National Hospitals Office.

Our multidisciplinary specialist treatment team has recently published our national management guidelines on the HSE website and we have appointed 2 clinical nurse specialists who with Dr John Coulter, clinical lead, will lead out and go "live" with our national registry in 2016.

Each new patient will be registered from each of the 19 obstetric units in the country and their weekly follow-up and management co-ordinated by the National registry team.

This initiative will lead to the expert specialist care of every woman with GTD in Ireland, integrating the different specialties of obstetrics, pathology, biochemistry, gynaecological oncology and medical oncology. With this expert specialist management these young women can expect cure rates of 95-99% in accordance with international best practice.

Session 4

Lectures to mark the International Year of Light



INTERNATIONAL
YEAR OF LIGHT
2015

LIGHT AND HEALTH

Chair:

Dr. Derek McKillop

Consultant Clinical Scientist, Southern Health and Social Care Trust, Craigavon, Northern Ireland

Dr. Andrew Coogan

Senior Lecturer and Department Head,
Maynooth University Department of Psychology

The dark side of light-at-night

Professor Antony Young

St. John's Institute of Dermatology,
King's College London

The risks and benefits of solar UVR exposure

Presentation of Geraldine Roberts Medal for best scientific poster

Conference close



Abbott
Diagnostics

Session 4

Dr. Andrew Coogan

**Senior Lecturer and Department Head
Maynooth University Department of
Psychology
Co. Kildare**



BIOGRAPHY

Dr. Coogan is a behavioural neuroscientist who specialises in the field of circadian rhythms, chronobiology and sleep. He is the director of the Chronobiology and Sleep Research

Laboratory at Maynooth University, as well as being Head of the Department of Psychology at Maynooth. His particular research interest is in how the fields of circadian clocks, immunology and psychiatry may overlap. He has a Bachelors degree from Trinity College Dublin and a PhD from University College Dublin. His PhD worked examined the links between the immune system and the processes thought to underpin memory formation. After completion of his PhD he was a post-doctoral research associate at the University of Manchester for five years prior to taking up a faculty position at the School of Medicine, Swansea University, where he spent another five years prior to joining Maynooth University in 2008. At Maynooth he teaches biological psychology, research methodology and statistics and advanced modules on sleep and circadian rhythms and comparative psychology on the undergraduate degree programme in psychology, as well as supervising undergraduate research projects and MSc/PhD research students. Dr. Coogan has published 51 peer reviewed papers in neuroscience to date in international journals (with >1,200 citations to date on Scopus; H-index of 21), is currently the Secretary of Neuroscience Ireland, is a member of several scientific societies and has been an invited speaker at a number of international conferences and symposia.

The dark side of light-at-night

Light has profound influences on multiple aspects of human physiology and behaviour. A key mechanism through which light exerts such effects is via modulation of the circadian timing system. This is an intrinsic biological timekeeping network that serves to impose a near twenty four hour temporal architecture on a myriad of molecular, physiological and behavioural processes. It is well established that light is the key environmental time cue (Zeitgeber) that serves to synchronise the circadian clock to external cycles, and thereby maintain the biological salience of the clock. From an anatomical perspective, the master clock of the circadian system is located to the suprachiasmatic nuclei (SCN) of the anterior hypothalamus.

The SCN itself receives direct retinal innervation from a subset of intrinsically photoreceptive ganglion cells expressing the photopigment melanopsin. Light at various times of the day causes alterations in circadian timing, in a manner that it dependent on the phase of the circadian cycle during which the light is presented. Until late into the 19th century, the presence or absence of environmental light was predominantly determined by the solar cycle. However, with the advent of electrical lighting, such environmental illumination is possible on a twenty four hour basis. This has the consequence that the circadian system may be consistently exposed to light at phases during which it would not be under natural photoperiods. This in turn may lead to chronic desynchronisation of the circadian network and adverse health outcomes.

Dysfunction of the circadian system is linked to common pathologies, including cancer, diabetes and cardiovascular disease, as well as psychopathologies. Human populations who are exposed to aberrant patterns of light exposure, such as shift workers, are found to be at higher risk of developing a number of chronic conditions, and nocturnal light-induced circadian disruption is believed to be an important mechanism in heightening such risks. In this talk I will highlight mechanisms through which artificial light-at-night may impact on human health and wellbeing, and illustrate how a fundamental understanding of the circadian system may lead to measure to ameliorate such risks.

Session 4

The risks and benefits of solar UVR exposure

Terrestrial solar UVR comprises UVB (~295–315nm) and UVA (315–400nm) radiation, the vast majority (>95%) being UVA. Skin exposure to sunshine causes damage at molecular, cellular and clinical levels. Molecular consequences include structural changes to DNA that may result in mutation, the generation of reactive oxygen species (ROS) and gene expression. Cellular changes include apoptosis, loss of epidermal antigen presenting cells and an inflammatory infiltrate. Sunburn (erythema) is the most obvious acute effect but UVR also suppresses the skin's acquired immunity. Skin cancer is the most important long-term effect, especially malignant melanoma, but chronic UVR exposure also induces photoageing: UVR activates the production of matrix metalloproteinases (MMP) that degrade the extracellular matrix of the dermis.

The most established benefit of solar UVR exposure is vitamin D synthesis. However, there is also evidence that UVR stimulates the skin's innate immunity and reduces blood pressure. Many people see tanning as a benefit but this is a consequence of molecular damage.

The numerous acute and long-term effects of the sun are initiated by UVR absorption of skin chromophores (e.g. DNA), each with a characteristic absorption spectrum. This spectrum, and its interaction with skin optics, determines the efficacy of a given wavelength to cause a given photobiological outcome. Efficacy vs. wavelength is known as an action spectrum. The most widely studied skin action spectrum is for erythema, which shows a peak at about 300nm; the consequence of which is that the <5% of UVB in solar UVR accounts for >80% of a summer sunburn. However, almost all action spectra of adverse effects show maxima in the UVB range; often more effective than UVA by orders of magnitude. This includes skin cancer and photoageing based on mouse studies. UVB is necessary for the synthesis of vitamin D. Long wave UVA (340–400nm) is responsible for the reduction of blood pressure.

It is important to protect the skin from UVB to mitigate its many adverse effects, but this must be done so as to enable vitamin D production.

Professor Antony R Young
Professor of Experimental
Photobiology
St John's Institute of Dermatology
Faculty of Life Sciences and Medicine
King's College London
London, UK

BIOGRAPHY

Professor Young has been involved in research on the effects of ultraviolet radiation (UVR) on human skin for the past 25 years. The European Commission (EC), UK Department of Health, UK Medical Research Council, research charities and industry have largely funded this research. Professor Young has a long-standing interest in photoprotection, and is also currently working on vitamin D, the photobiology of different skin types and the development of natural marine sunscreens. He was recently the coordinator of a 4-year EC €4.5-million research project, within its Framework 7 Environment and Climate Change Programme, entitled "The impact of climatic and environmental factors on personal ultraviolet radiation exposure and human health". This multi-national project assessed the beneficial and detrimental health impacts of UVR in field studies of human populations in work and leisure situations in different European countries.

Professor Young is an active member of the American Society for Photobiology (ASP) and the European Society for Photobiology (ESP). He is currently an associate editor of Photodermatology, Photoimmunology and Photomedicine and section editor of the Journal of Dermatological Science. Professor Young is also a member of the United Nations Environment Programme (UNEP) – Environmental Effects Assessment Panel (EEAE). He is also a member of the Advisory Group on Non-ionizing Radiation (AGNIR) working on a review of UVR in relation to vitamin D synthesis. AGNIR reports to Public Health England (PHE).

1. Vitamin D supplementation in Obstructive Sleep Apnoea Syndrome

K. Hutchinson^{1,3}, C. Kerley^{2,4}, Y. Rochev³, M. Louw¹, J. L. Faul^{2,4}, L. Cormican^{2,4}

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³NCBES, National University of Ireland, Galway, Ireland

⁴UCD, Dublin 4, Ireland

2. Methodological variation of common vitamin D assays for the assessment of 25-hydroxyvitamin D concentration and impact on classification of status

E. Laird¹, M. Ward², H. McNulty², M. Healy³, J. Wallace², K.D. Cashman⁴, E. McSorley², T. Hill⁵, G. Horgan², L.K. Pourshahidi², M.S. Mulhern² & JJ Strain^{2*}

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⁵School of Agriculture, Food & Rural Development, Newcastle University, Newcastle NE1 7RU, United Kingdom

3. The potential of geomapping for visualising vitamin D status in the St. James's catchment area

T Shannon¹, E Laird², M Redha¹, Crowley VEF¹, Healy M¹

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4. Faecal Elastase: Requesting patterns and results over a 5-year period in St. James's Hospital, Dublin

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

5. Evaluation of a fully automated Immunoassay Method for the determination of Anti-Mullerian Hormone and comparison with an enzyme linked immunosorbent assay

John Lyne, Mark Neville, Dr. Vivion Crowley
Biochemistry Department, St. James Hospital, Dublin 8

6. Establishment of reference intervals for sex hormone binding globulin and LC-MS/MS derived free androgen index & free testosterone

MR Cullen, SN Duignan, KJ Mulready, JJ Brady, MM MacMahon, MC Fitzgibbon

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

7. An Audit on the Prevalence of Macroprolactin as a cause of hyperprolactinaemia

MR Cullen, SN Duignan and MC Fitzgibbon

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

8. Preanalytical Delays and Gestational Diabetes

Mary Stapleton, Ruth O'Kelly

Coombe Women and Infants University Hospital, Dublin 8

9. From Audit to Diagnostic Algorithm – A Search for the Best Tests for Diabetes Screening in High Risk Patients.

Peadar McGing¹, Maria Fitzgibbon¹, Claire Gavin²

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²Mater Misericordiae University Hospital, Department of Endocrinology, Dublin, Ireland

10. When is a wrong result a good result?

Paudy O'Gorman¹, Peadar McGing², Joan Dinneen¹, Ger Collier³, Colman O'Loughlin⁴, Adrian Moughty⁵, Maria Fitzgibbon²

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³Toxicology Department, Beaumont Hospital,

⁴Intensive Care Unit, MMUH,

⁵Emergency Department, MMUH

11. Achieving best practice in oncology – Is cystatin C an alternative biomarker to creatinine in assessing renal function?

Melissa Jones, Stephanie Denieffe, Maria Fitzgibbon

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

12. Assessing renal function in oncology – Is our loyalty to established methods compromising accuracy?

Melissa Jones, Stephanie Denieffe, Maria Fitzgibbon

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

13. Reference Ranges Revisted

Lee GR, McGing P and Fitzgibbon M
Department of Clinical Biochemistry and Diagnostic
Endocrinology,
Mater Misericordiae University Hospital (MMUH), Dublin

14. Clinical and Biochemical Features of Four Patients with Short Chain Enoyl-CoA Hydratase Deficiency a Defect in Valine Metabolism – Irish Experience

Fitzsimons PE¹, Hughes J², Crushell E², Twomey E³, Walsh R¹, Taylor RW⁴, Ruiter JP⁵, Ferdinandusse S⁵, Wanders RJA⁵, Pitt JJ⁶ and Mayne PD¹

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15. From Finger Prick to Finger Tip – Phenylalanine Results by Text for Patients with PKU

Deverell D¹, O'Shea A¹, Trench C¹, Kelleher U¹, Clark A², Macauley M², Branagan P³, Rourke M³ and Newcombe N³

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²National Centre for Inherited Metabolic Disorders,

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16. Evaluation of the performance of a revised hypoglycaemia work-up in infants and children

Erum Rasheed, Colm Carolan, Philip Mayne
Department of Paediatric Laboratory Medicine, Temple Street
Children's University Hospital, Dublin 1

17. Development of a tandem mass spectrometry method for total and free carnitine analysis and comparison of acylcarnitine profiles from patients on ketogenic diets using plasma and dried blood spot assays

Caroline Murray¹, Patricia Fitzsimons¹, Nicola Finnegan¹, Prof. Mary King² and Philip Mayne¹

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Temple St. Children's University Hospital,

²Department of Neurology, Temple St. Children's University Hospital, Dublin

18. The Validation of an Anti-Müllerian Hormone assay and an investigation into its uses to support a fertility clinic

Conor Lucey¹, Damian Lally², Marie Culliton²

¹Dublin Institute of Technology,

²The National Maternity Hospital

19. The Alpha-1 Antitrypsin Deficiency National Targeted Detection Programme

L. Fee, T.P. Carroll, C. O'Connor, P. O'Brien¹, E. Pentony¹, I. Ferrarotti², S. Ottaviani², M. Luisetti², W. Tormey¹, and N.G. McElvaney

Alpha One Foundation, RCSI Education & Research Centre,
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20. γ -Secretase Cleavage of TNFR1 mediates the segregation of TNF α -induced survival and pro-apoptotic pathways

Caroline Coleman Vaughan, Jyoti Chhibber, Stephen Duggan, James Powell and Justin V. McCarthy
School of Biochemistry & Cell Biology, ABCRF, University College
Cork, Cork, Ireland

21. Very low serum HDL-cholesterol due to malaria? – a case report

Ana Rakovac Tisdall¹, Aftab Khattak², Kyaw Zaw Linn³, Niamh Dever¹, Badriya Al-Alawi¹, Vivon Crowley¹

¹Department of Biochemistry, St. James's Hospital, Dublin 8,

²Department of Endocrinology, St. James's Hospital,

³Department of Medicine, St. James's Hospital

22. Clinical audit of the genotypic frequencies of Hereditary Haemochromatosis referrals to Cork University Hospital 2009-2012

McDonald, C¹, Joyce, C¹, Su, Y²., Crosbie, O¹

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Cork University Hospital

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Poster 1

Vitamin D supplementation in Obstructive Sleep Apnoea Syndrome

K. Hutchinson^{1,3}, C. Kerley^{2,4}, Y. Rochev³, M. Louw¹, J. L. Faul^{2,4}, L. Cormican^{2,4}

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INTRODUCTION:

Our group and others have reported a high rate of vitamin D deficiency in obstructive sleep apnoea syndrome (OSAS)^{1,2}, where vitamin D levels (25(OH)D) correlate negatively with apnea-hypopnea index (AHI) and glucose metabolism.^{3,4}

DESIGN AND METHOD:

In Autumn/Winter 2013 we recruited 26 adults (20 male), aged $55.2y \pm 12$, BMI: $30.4 \text{ kg/m}^2 \pm 5.6$ with nocturnal polysomnogram (PSG) proven OSAS.

70% were stable, long term continuous positive airway pressure (CPAP) users.

At baseline we assessed: Quality of life (QoL) with the Epworth Sleepiness Scale (ESS) and the Sleep Apnoea Quality of Life Inventory (SAQLI), neuropsychological function with trail making tests and Connor's Continuous Performance Test II (CPT II).

25(OH)D, calcium, PTH, phosphate, hsCRP, Cholesterol, LDL, Insulin, HDL, Lipoprotein associated phospholipase A2 (PLAC) and fasting glucose were measured using an Abbott Architect ci8200.

The intervention was 15 weeks of 4,000 iu vitamin D3/day or matching placebo.

RESULTS:

There were no CPAP or medication changes. CPAP compliance was high (~93%)

There were 7 dropouts, leaving 19 subjects who completed all assessments.

There were no differences between the vitamin D and placebo groups at baseline.

Mean baseline 25(OH)D was 37.2nmol/L (range: 15-87). According to the *Institute of Medicine* guidelines, 17 (89%) were vitamin D deficient (25(OH)D <50nmol/L), while 2 (11%) were vitamin D sufficient (25(OH)D >50nmol/L).

CONCLUSIONS

In conjunction with a significant increase in 25(OH)D levels ($p=0.00003$),

vitamin D supplementation was associated with improved quality of life, as well as metabolic and neuropsychological indices compared to placebo.

Vitamin D replenishment warrants further investigation as an adjunct therapeutic strategy in OSAS.

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Poster 2

Methodological variation of common vitamin D assays for the assessment of 25-hydroxyvitamin D concentration and impact on classification of status

E. Laird¹, M. Ward², H. McNulty², M. Healy³, J. Wallace², K.D. Cashman⁴, E. McSorley², T. Hill⁵, G. Horigan², L.K. Pourshahidi², M.S. Mulhern² & JJ Strain^{2*}.

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BACKGROUND:

There is considerable debate as to which methodology is the most sensitive and accurate for the analysis of circulating 25(OH)D concentration given the reported variability between different assays. Currently, no study has investigated this issue in individuals exposed to higher vitamin D intakes through supplementation compared to the lower intake levels encountered through normal dietary exposures.

METHODS:

Stored samples from healthy adults (aged 20-40 years (n 102) and >64 years (n 117)) who were participants in a previous vitamin D intervention trial were available for re-assessment of 25(OH)D status. Serum concentrations of 25(OH)D were quantified using LC-MS/MS (Chromsystems) and compared to results originally obtained by enzyme immunoassay (IDS EIA) using Bland-Altman analysis.

RESULTS:

Compared to LC-MS/MS, the EIA method overestimated 25(OH)D concentrations by 2.9 nmol/l / +8.2%. Below the reference cut-off for sufficiency (<50 nmol/l) the EIA method generated values that were on average 12.1nmol/l / +26.5% greater than LC-MS/MS while at ≥50 nmol/l, values obtained using EIA was on average 6.4nmol/l / -10.3% lower than LC-MS/MS. Both pre and post supplementation (D3), significantly more participants were defined as sufficient by EIA in comparison to LC-MS/MS (Pre 48% vs. 38%; P=0.034; Post 72% vs 56%; P=0.003).

CONCLUSION:

This study provides clear evidence that choice of method can have a significant impact on the classification of vitamin D status in human studies and for public health purposes. The findings suggest that until methodologies are standardized, defining vitamin D status using a single universal cut-off point is inappropriate.

Poster 3

The potential of geomapping for visualising vitamin D status in the St. James's Hospital catchment area

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²Institute of Molecular Medicine, Trinity College Dublin

INTRODUCTION:

Vitamin D deficiency (25(OH) D \leq 30 nmol/l) is a significant global health concern. Determinants of vitamin D include ethnicity, economic status, season and geographic location. The potential mining of laboratory data could have benefits for the analysis of vitamin D status and the possible development of tools for evaluating epidemiological trends in defined population areas. The purpose of this pilot study is to graphically visualise vitamin D data for the St. James's Hospital catchment area using the process of geomapping.

METHODS:

The catchment area of St. James's Hospital includes all or part of Dublin 2, 6, 8, 10, 14, 16, 20, 24, Dublin County (mainly Lucan) and County Kildare (mainly Leixlip). A search was conducted using the Biochemistry Department LIMS for vitamin D requests by GPs in these areas. Samples requested between January and December 2014 were selected. The search parameters for this query included the patients address and postcode. Results were tabulated according to median values for vitamin D in each postal district as well as the percentage of samples deficient, insufficient or normal.

Analysis of vitamin Ds was performed using liquid chromatography-triple quad mass spectrometry (API 4000, ABSciex USA). Exclusion criteria included patients < 18 years, missing demographic data, unknown addresses or nursing home locations.

RESULTS:

A total of 4,269 GP samples were received for vitamin D requests in the time period studied. Of these, 1863 were collected in the winter months. The results below reflect the winter samples. The median vitamin D concentration ranged from 47.0 nmo/l (Dublin 2) to 73.0 nmol/l (Dublin 18). Areas with the greatest percentage of deficient vitamin D concentrations (< 30nmol/l) were Dublin 2 (24%), Dublin 8 (24%), Dublin 4 (21%), Dublin 20 (21%) and Lucan (20%). Combined percentages for those with deficient (<30 nmol/l) and insufficient (30-50 nmol/l) concentrations showed that Dublin 2 had the highest overall rate of abnormal vitamin D levels (61%) with Dublin 6W showing the lowest (30%). The percentage of those with vitamin D sufficiency (> 50nmol/l) was lowest in Dublin 2 at 39% and highest in Dublin 6W at 70%.

CONCLUSION:

The data generated in this study will be graphically visualised using geomapping of the Dublin postal districts. This, along with sociological data, will give a picture of vitamin D status and possible confounding factors in the St. James's Hospital catchment area. There is the potential to inform public health policy regarding endemic vitamin D deficiency/insufficiency across large sections of society using this procedure.

Poster 4

Faecal Elastase: Requesting patterns and results over a 5-year period in St. James's Hospital, Dublin

James Kelly, Vivion Crowley, Martin Healy

Biochemistry Department, Central Pathology, St. James's Hospital, Dublin 8

INTRODUCTION:

Several conditions including cystic fibrosis and diabetes mellitus can result in exocrine pancreatic insufficiency (EPI) eventually leading to severe maldigestion and malabsorption. Early biochemical investigations of exocrine function employed invasive tests such as the Secretin-CCK test. Highly sensitive and considered a gold standard this test, however, has some serious drawbacks. It is time consuming, expensive, uncomfortable, not standardised and requires peroral placement of a tube into the duodenum.

Faecal elastase (FE) was introduced into the biochemistry department in 2005 as an indirect non-invasive test of EPI. Elastase is a pancreatic enzyme involved in degradation of connective tissue protein. It has several advantages that support its use as a reliable marker of EPI. It is transported down the intestine bound to bile salts after pancreatic release. It is not degraded during its transit. It is concentrated 4 to 5 times in faeces. It is stable at room temperature for up to a week and is quantitated using a simple monoclonal antibody ELISA. The assay has excellent correlation with the Secretin-CCK test. Sensitivity and specificity of FE for moderate and severe EPI is 90-95%. For mild disease it has been estimated at 63%. A stool value of <100, 100-200 and >200 µg/g indicates severe, mild to moderate and normal values when interpreting analysis of EPI.

METHODS:

A 5-year gather (2011-2015) was performed on the biochemistry department LIMS. Search criteria were name, age, sex, location (ward/hospital), clinical details and result. The ELISA kit used for analysis was supplied by ScheBo Biotech AG, Giessen.

RESULTS:

A total of 1408 results were analysed in the 5-year period. On average FE requesting is increasing by 10% per year. The age range was 11-90 years. 58% of patients were male and 42% female overall. Taking this population as a whole (male + female) 26% of results were in the severe or mild to moderate FE range. Breaking down the data into female and male results in the total sample, however, demonstrated that a greater number of males (32%) than females (19%) had abnormal findings. The mean concentration of FE, though, remained similar for the cut-offs between the 2 groups e.g. mean concentration for the <100 µg/g faeces group was 39.8 ± 2.2 SEM for males (n=159) and 35.3 ± 1.8 SEM for females (N=63). The 51-70 yrs age group had the greatest number of requests for FE (46% for males n=813 and 42% for females n=595).

CONCLUSIONS:

The FE assay is easy to perform and robust. It is CE marked and EQA schemes are available. It is an excellent indicator of moderate and severe EPI with somewhat lower sensitivity for mild disease, reflecting the large reserve capacity of the pancreas. The population described refers to symptomatic referrals to SJH and FE has proved a valuable aid in assessing EPI. It appears from this sample that males have a higher prevalence of EPI particularly in the 51-70 yrs age group. This needs to be confirmed with larger population studies. FE values can be used as a guide to commencing enzyme replacement therapy in the presence of malabsorption. The ScheBo assay is unaffected by the enzymes used in this treatment. SJH is the only hospital providing a routine service for this test in the Republic. The assay is fully accredited and the lab accepts samples for analysis from other centres.

Poster 5

Evaluation of a fully automated immunoassay method for the determination of Anti-Mullerian Hormone and comparison with an enzyme linked immunosorbent assay

John Lyne, Mark Neville, Vivion Crowley

Biochemistry Department, St. James Hospital, Dublin 8

INTRODUCTION:

AMH is a useful marker of ovarian reserve and can be used to assist in optimizing in vitro fertilization treatment. AMH was traditionally assayed by a non-automated enzyme linked immunosorbent assay (Beckman Coulter AMH Gen II ELISA). However, this technique has many associated technical problems. This research aims to extensively validate a newly introduced automated assay for AMH (Roche Elecsys®/cobas), including comparisons with the non-automated ELISA method.

METHODS:

The validation of the methods involved both direct assessment of various performance characteristics of the assays and method comparisons using multiple patient samples (n=42) from external laboratories. Temperature stability and interference studies were also undertaken using patient samples (n=7). Clinical utility of the validated Roche AMH assay was assessed in female patients undergoing cancer treatment (n=4).

RESULTS:

Both assays were linear to 122 pmol/L, with $R^2 = 0.9889$ and $R^2 = 0.996$ for the Beckman Coulter and Roche methods respectively. Intra-assay imprecision was lower for Roche (CV=0.6%) compared with Beckman Coulter (CV=5.22%). In addition, accuracy was assessed using EQA samples and all results were within 14% (Beckman-Coulter) and 5.3% (Roche) of target values. Inter-assay imprecision of the Roche method was assessed using IQC material and reported CV=5.55% (lower level) and 4.14% (higher level). The lower limit of quantitation in the Roche assay concurred with the manufacturer's recommendations.

The three method comparisons carried out in this study all showed close agreement. This included (1) Beckman Coulter AMH method – host laboratory versus external laboratory ($r=0.965$), (2) Comparison of Roche and Beckman Coulter using external laboratory samples ($r=0.986$) and (3) Roche AMH method – host laboratory versus a second external laboratory ($r=0.991$). Sample stability was confirmed at -20°C, 4°C and room temperature, while haemolysis at varying levels did not cause interference.

CONCLUSION:

The Roche Elecsys®/cobas automated method for AMH analysis has many advantages over the traditional, manual ELISA methods. Overall it has superior performance characteristics and is robust, fast, accurate and reproducible, therefore improving the clinical utility of the results.

Poster 6

Establishment of reference intervals for sex hormone binding globulin and LC-MS/MS derived free androgen index & free testosterone

MR Cullen, SN Duignan, KJ Mulready, JJ Brady, MM MacMahon, MC Fitzgibbon

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OBJECTIVE:

Last year, a LC-MS/MS total testosterone assay was introduced into clinical practice at the Mater Misericordiae University Hospital. Analysis of the sex hormone binding globulin (SHBG) and calculating either the free androgen index (FAI) or the free testosterone (cFT) is used to support the interpretation of clinical equivalent testosterone concentrations. SHBG is utilised in both of these calculated parameters. Recently, a 2nd WHO international standard (IS) (08/266) was established to replace the 1st IS (95/560). Our aim was to establish reference intervals traceable to this new IS for SHBG. In addition, new reference intervals for the FAI and cFT were also determined.

STUDY DESIGN:

One hundred and seven females and 63 males with an age range spanning 18 to 86 years were analysed. Testosterone was measured by LC-MS/MS and SHBG by immunoassay on an Abbott Architect. The FAI was used to determine free testosterone in females and the Vermeulen equation was used to determine the cFT in males.

RESULTS:

The SHBG reference intervals for females and males were 24 – 185 nmol/L and 8.8 – 78 nmol/L respectively. The reference interval for the female FAI and male cFT were 0.43- 4.6% and 0.13- 0.55 nmol/L respectively.

CONCLUSIONS:

We are the first large study to report reference intervals for SHBG calibrated to the 2nd WHO IS. In addition, this is the first large study to establish FAI and cFT using both this new SHBG IS and using testosterone as analysed by LC-MS/MS.

Poster 7

An Audit on the Prevalence of Macroprolactin as a cause of Hyperprolactinaemia

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OBJECTIVE:

At the Mater Misericordiae University Hospital (MMUH), prolactin is analysed by immunoassay on an Abbott Architect platform. This assay has been shown to detect biologically inactive macroprolactin. The presence of macroprolactin at high concentrations may result in hyperprolactinaemia. This could lead to misdiagnosis or unnecessary additional investigations. We routinely screen all hyperprolactinaemic patients for macroprolactin using PEG precipitation. The aim of the study was to determine the prevalence of macroprolactin at MMUH.

STUDY DESIGN:

A gather from January 2014 to June 2015 was performed to collate all prolactin requests. Samples with prolactin greater than > 600 mIU/L for females or > 550 mIU/L for males were reflexed, at the time of analysis for PEG precipitation. The presence of macroprolactin was defined as, a recovery of less than 40% prolactin after PEG precipitation.

RESULTS:

There were 5617 prolactin requests over the 18 month period. Fifty eight percent, 12% and 30% of the requests were from primary care, MMUH medical teams and referral hospitals respectively. Eighty five percent of all requests were female. Macroprolactin was analysed in 674 (12%) of the total requests and was detected in 95 (14%) of samples. Forty (6%) of these patients with macroprolactin had also a raised monomeric or bioactive prolactin.

CONCLUSIONS:

Our audit is in agreement with literature, which reports macroprolactin as a cause hyperprolactinaemia as analysed by Abbott Architect to be approximately 17%. The screening protocol to detect macroprolactin at MMUH reduces misdiagnosis and unnecessary costly follow up investigations.

Evaluation of the Toxic Risk of Fluoropyrimidines & Determination of 5-fluorouracil (5-FU) in Patients with Cancer

5-fluorouracil (5-FU) and orally available 5-FU prodrugs are central to almost 60% of chemotherapy protocols (in particular for digestive, oropharyngeal, breast and pancreas cancers). The use of these drugs can produce severe and unpredictable side effects which have been mainly attributed to a deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD). It is estimated that 3–5% of patients carry mutations in the *DPYD* gene which influence DPD activity. Pretherapeutic detection of this metabolic dysfunction reduces the patient's risk of toxicity or of therapeutic inefficacy. Biomnis Ireland is delighted to announce that the following tests are now available through our laboratories:

EVALUATION OF THE TOXIC RISK OF FLUOROPYRIMIDINES BY A MULTI-PARAMETRIC APPROACH (5FU^{ODPM TOX}) (BEFORE TREATMENT)

This test enables the risk of fluoropyrimidine toxicity to be evaluated and the determination of the dose to be administered

in the first cycle, thanks to its multi-parametric approach combining:

- screening for gene mutations that influence dihydropyrimidine dehydrogenase (*DPYD*);
- determination of uracil (U) and dihydrouracil (UH2);
- consideration of the patient's pathophysiological parameters.

DETERMINATION OF 5-FLUOROURACIL FOR DOSE ADJUSTMENT (5-FU^{ODPM} PROTOCOL) (DURING TREATMENT)

This test enables the dose to be calculated as a function of pharmacokinetic, physiological and pathophysiological parameters and of the characteristics of the chemotherapy protocol during the entire duration of treatment.

If you would like further information regarding the above tests please contact your local hospital laboratory or Biomnis Ireland on (01) 295 8545 or sales@biomnis.ie

Poster 8

Preanalytical delays and Gestational Diabetes

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Gestational diabetes mellitus (GDM) is a disorder of glucose intolerance occurring for the first time in pregnancy. Associated with increased foetal and maternal morbidity, a diagnosis of GDM also identifies women at increased risk of developing type 2 diabetes in the future.

Although the landmark Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study standardised preanalytical requirements for samples used to diagnose GDM, guidance issued by the HSE does not include this as a requirement.

The aim of this study was to examine the effects of glycolysis on samples received for glucose analysis, and determine what effect, if any, it would have on rates of GDM diagnosis.

Samples were received as recommended by the HAPO study, and measured immediately. Aliquots of the samples were removed at receipt and incubated at either room temperature or in ice for a standardised period of time prior to separation and analysis.

Of 192 fluoride-EDTA samples received on ice, there was an average decrease of 0.4mmol/L glucose concentration after 2.5 hours. When fluoride-EDTA samples were held on ice for 2.5 hours, there was a decrease of 0.2mmol/L in glucose concentration.

The study was extended to include lithium heparin samples received in the same manner as the fluoride tubes. Two and a half hours at room temperature and on ice caused an average decrease in glucose concentration of 0.8mmol/L and 0.2mmol/L respectively.

If routine samples were treated as indicated by the HAPO study, it is likely that the rates of GDM diagnosis in CWIUH would rise. This increase in diagnosis and related costs would hopefully be offset by the prevention of adverse outcomes in both mother and baby.

The accuracy of glucose measurement is vital in the diagnosis of gestational diabetes, as a diagnosis directs the treatment and monitoring of women to minimise effects of uncontrolled glucose levels.

Poster 9

From Audit to Diagnostic Algorithm – A Search for the Best Tests for Diabetes Screening in High Risk Patients

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BACKGROUND:

The oral Glucose Tolerance Test (oGTT) is the classical test for diagnosing Diabetes Mellitus (DM). In recent years HbA1c has also been approved as a diagnostic test. We previously investigated concordance between the oGTT tests, Fasting Plasma Glucose (FPG) plus 2 hour Glucose (2hGlu), and HbA1c, using two years of data (7/2010 to 6/2012).

OBJECTIVE:

The aim of this study was to derive and verify a practical algorithm for diagnosis of DM in non-acute patients considered at increased risk of DM.

METHODS:

For the Verification Study the Laboratory Information System (LIS) was interrogated for all oGTTs performed within ± 3 days of HbA1c test for one year (7/2014 to 6/2015; n=285). Glucose load for oGTT was 75g anhydrous glucose in 300mL water (Dr Reddy's Laboratories powder, made up in-house (6/2014-11/2014); RapiLOSE® (11/2014-6/2015)). 'Acute' was defined as in-patient, 'Non-acute' as GP or out-patient.

RESULTS:

We propose screening using HbA1c plus FPG as front-line, with oGTT performed in selected patients. From our 2010/12 data we determined the following gave best results in respect of not missing DM while not requiring inappropriate levels of oGTTs.

DIAGNOSTIC ALGORITHM:

Screen all patients for FPG and HbA1c. If $FPG < 5.6$ mmol/L and $HbA1c < 42$ mmol/mol \rightarrow normal (no further testing unless strong clinical suspicion); if $FPG > 6.9$ or $HbA1c > 47 \rightarrow$ DM; all others proceed to oGTT. When applied to all non-acute patients the algorithm had sensitivity for DM of 95% and specificity for DM/Pre-DM of 80% (97% and 62% for GP patients).

DISCUSSION:

There is a lot of confusion in the literature and in routine practice concerning the optimal testing strategy for diabetes. In the UK the NICE guideline for DM-Type2 risk identification recommends using $FPG < 5.6$ or $HbA1c < 41$. We propose using these two tests at those limits but in combination instead of as alternatives. This gives greater sensitivity for DM while still limiting need for oGTTs.

Poster 10

When is a wrong result a good result?

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CASE PRESENTATION:

A 53 year old lady was brought by ambulance to MMUH ED at 14.46 on Sunday 1-2-15. On presentation: GCS=4, profoundly acidotic (pH=7.06), with evidence of high lactate (19.0 mmol/l; Radiometer ABL 90 Flex Blood Gas analyser in ED): Urea=45 mmol/l, Creat=143 µmol/l, K=6.0 mmol/l and Na=143 mmol/l. History suggested potential deliberate self-harm. There was no evidence of hypoperfusion in spite of the high lactate. Lactate increased to 24.0 mmol/l (Radiometer) 4 hours after presentation. Ethylene Glycol analysis was requested 4.6 hours after presentation. The patient was transferred to ICU with working diagnosis of Benzodiazepine overdose.

ICU bloods (8 hours post presentation): Urea=6.3, Creat=216. A blood gas sample was analysed in ICU (Nova pHox Ultra) pH=7.332 and Lactate=2.3 mmol/l. 33 hours after presentation urinary output had decreased significantly; Urea=12.1, Creat=505, pH=7.332, lactate=1.7 mmol/l. Dialysis commenced in ICU 35 hours after initial presentation.

Toxicology was reported 48 hours after the patient presented: Ethylene Glycol (EG) undetectable (>40 mg/l) but strongly positive for Glycolic Acid (991 mg/l) – a breakdown product of EG. Clinicians subsequently queried potential Lactate Gap, i.e. apparent discrepancy in lactate results.

LABORATORY INVESTIGATIONS:

A pool of whole blood was collected and divided into three sub-pools.

A: baseline, B and C: baseline spiked with 500 and 1,000 mg/L Glycolic Acid respectively. Lactate was measured in each sub-pool (n=5) using Radiometer ABL 90 Flex and Nova pHox Ultra analysers.

Mean lactate results (mmol/L):

Radiometer: A=6.0, B=14.9, C=20.4. Nova: A=5.7, B=4.8, C=4.1.

DISCUSSION:

The results obtained in this study reflected the findings in the patient sample, confirming the ability to determine a ‘lactate gap’ by measuring a sample on both of our in-house blood gas platforms. The patient remains on intermittent haemodialysis awaiting transplant.

Detection of a Lactate Gap allows presumptive diagnosis of EG poisoning. Awareness of the lactate gap would have resulted in dialysis being instigated some 30 hours earlier in this case which may have increased preservation of renal function.

Poster 11

Achieving best practice in oncology – Is cystatin C an alternative biomarker to creatinine in assessing renal function?

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OBJECTIVES:

Creatinine levels are routinely monitored in oncology patients to assist in evaluating renal function, however factors such as changes in muscle mass and dietary protein intake can independently affect levels. This study aimed to compare creatinine measurements with cystatin C which has been promoted as a suitable alternative.

STUDY DESIGN:

Eighty-four oncology patients (M: 18, F: 66) were prospectively recruited, with a serum sample taken prior to commencing each chemotherapeutic cycle. Creatinine was measured using an enzymatic assay and cystatin C by an immunoturbidometric assay (Abbott Diagnostics). Estimated GFR (eGFR) was calculated by Modified Diet in Renal Disease (MDRD) and Chronic Kidney Disease-Epidemiology collaboration (serum creatinine) (CKD-EPI SCr) equations.

RESULTS:

Creatinine measures in oncology patients were comparable with a normal population throughout chemotherapy treatment. In contrast, patients demonstrated elevated levels of cystatin C when compared with a normal population prior to and during chemotherapy (males and females respectively, $p < 0.0001$, Kruskal-Wallis). Furthermore, cystatin C measures increased significantly during the course of chemotherapy in female patients ($p < 0.02$, Friedman). Breast and lung cancer patients (females) demonstrated elevated levels of cystatin C when compared with a normal female population ($p < 0.0001$, Kruskal-Wallis). No significant difference in creatinine-based estimated GFR was noted during treatment ($p > 0.05$, Friedman).

CONCLUSION:

The elevated levels of cystatin C identified in this oncology cohort are suggestive of a malignancy and treatment-mediated effect on cystatin C levels, which would diminish its utility in this patient population. When combined with stable creatinine and eGFR measures, the findings from this study promote the maintenance of creatinine assessment, given appropriate monitoring of muscle mass and patient diet.

Poster 12

Assessing renal function in oncology – Is our loyalty to established methods compromising accuracy?

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OBJECTIVES:

Oncology patients receiving chemotherapy require close monitoring of kidney function to promptly detect renal impairment. This study aimed to evaluate the renal assessment formulae Cockcroft-Gault (CG) used by pharmacy and the Modified Diet in Renal Disease (MDRD) formula used by laboratories and to compare with Chronic Kidney Disease-Epidemiology collaboration (CKD-EPI) equations, particularly in the area of chemotherapeutic agent dosing using the Calvert formula.

STUDY DESIGN:

A total of 84 oncology patients (M: 18, F: 66) were prospectively recruited. A serum sample collected prior to commencing each chemotherapeutic cycle was assessed for serum creatinine (SCr) using an enzymatic assay and for cystatin C (CysC) using an immunoturbidometric assay (Abbott Diagnostics). Creatinine clearance (CrCl) estimated by CG and estimated glomerular filtration rate (eGFR) measures determined by MDRD and CKD-EPI equations (SCr, CysC, SCr/CysC) were compared for each patient prior to commencing treatment and up to the 8th chemotherapeutic cycle. The Calvert formula was used to calculate carboplatin doses based on the CG and CKD-EPI SCr equations.

RESULTS:

MDRD demonstrated significant variation when compared with CG and CKD-EPI between eGFR values of 60-90 ml/min/1.73m² ($p < 0.0001$, Kruskal-Wallis). CG revealed significant discordance with CKD-EPI SCr, which resulted in considerable variation when calculating carboplatin doses (Bland-Altman, 95% limits of agreement: -135.5-99.24; 18% negative bias, SD: 59.89). All CKD-EPI formulae performed comparably.

CONCLUSION:

This study demonstrates a lack of concordance between CG and MDRD formulae when compared with CKD-EPI, which is suggestive of imprecision in the assessment of renal function in oncology patients. The significant discordance in carboplatin doses calculated by CG and CKD-EPI demonstrates that there is inaccuracy in current pharmacy practice. Furthermore, our findings support the adoption of CKD-EPI, in keeping with the evidence base that eGFR based on this formula is most closely aligned to gold standard measured GFR techniques.

Poster 13

References Ranges Revisited

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INTRODUCTION:

In 2011 our laboratory determined a comprehensive list of method-specific reference ranges (RRs) across our chemistry and immunoassay test repertoire. When a laboratory changes the pre-examination or examination procedure, RRs should be reviewed and changed when they are no longer relevant for the population served (ISO15189:2012, 5.5.2). Transference Validation studies, as recommended by the IFCC/CLSI, are often used for this purpose, typically when laboratories are changing analytical platforms. We have evaluated the current validity of our previously established RRs, as well as harmonized reference ranges, for a group of chemistry tests where there was no (known) methodological change over this 3 year period.

METHODS:

Method-specific reference ranges (RRs) were determined previously (2012) using serum obtained from volunteers (Male + Female, n>120) attending a hospital health-check session. From a similar healthy cohort, serum (n>20) samples were used subsequently (2014) to evaluate the validity of our established RRs for 8 chemistry tests: Na, K, Cl, PO₄, Mg, Urea, Albumin and Total Protein. RRs were considered valid when <10% of data were outside the reference interval. All samples were analysed on Abbott ARCHITECT c16000 chemistry analysers. RR and validation studies were in accord with IFCC/CLSI guidance¹. Validation results were interpreted in part from longitudinal assessment of EQA data (2011-2014) and compared to RRs quoted by Abbott Diagnostics (AD) and Pathology Harmonization (PH).

RESULTS:

For Na, K, Cl, urea, albumin and total protein there were <2/20 results (<10%) outside of their respective method specific RR, supporting the validity of our established RRs. However, for albumin, Mg and PO₄ there were 3, 4 and 6 samples, respectively, outside of these ranges (i.e. >10%). Such results were lower than our quoted Lower Reference Limit (LRL) for albumin and Mg but higher than our Upper Reference Limit (URL) for PO₄. EQA data supported this observation for albumin (only), where there was a bias shift (+ve to -ve) during this 3 year time period. When the RR's confidence intervals (CIs) were considered, all tests had <10% of results outside of the CIs. By contrast, for evaluations against PH's RRs, most tests (6/8) showed no results outside of these quoted RRs.

CONCLUSION:

The IFCC/CLSI offer a simple approach to validating the transference of RRs. However, laboratories must fundamentally consider the appropriateness of the RR itself and its derivation before either proceeding to or concluding from transference studies and so avoid perpetual use of RRs which are irrelevant to the population(s) served.

Poster 14

Clinical and Biochemical Features of Four Patients with Short Chain Enoyl-CoA Hydratase Deficiency: A Defect in Valine Metabolism – Irish Experience

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INTRODUCTION:

Leigh Disease (LD) is a progressive, neurodegenerative disease presenting in early childhood with bilateral symmetric brain lesions. Non-specific biochemical findings include increased lactate in CSF and blood, increased Tricarboxylic acid cycle intermediates in urine and, often, deficiencies in mitochondrial respiratory chain complexes. Lack of specific bio-markers can make the diagnosis and genetic counselling particularly challenging.

Two enzyme deficiencies in the valine pathway have recently been described in LD: 3-Hydroxy-isobutyryl-CoA hydrolase (HIBCH), a mitochondrial enzyme catalysing the fifth step of valine catabolism, the conversion of 3-hydroxy-isobutyryl-CoA to 3-hydroxy-isobutyrate and short chain enoyl-CoA hydratase deficiency (SCEH / ECHS1), a mitochondrial enzyme that converts unsaturated trans- 2-enoyl-CoA species to the corresponding 3(S)-hydroxyacyl-CoA.

CASE PRESENTATION:

We describe four patients from two consanguineous families (one Pakistani, one Irish Traveller) who presented in infancy with LD. All had overlapping clinical features, developmental delay/regression, failure to thrive, hypotonia, seizures and apnoeic episodes.

RESULTS:

Urine organic acid analysis by GC/MS showed increased levels of *erythro*-2,3-dihydroxy-2-methylbutyrate and 3-methylglutaconate. Increased urine excretion of methacrylyl-CoA and acryloyl-CoA related metabolites analysed by LC-MS/MS were highly suggestive of ECHS1 deficiency. SCEH enzyme activity was markedly reduced in fibroblasts and both families were shown to have homozygous ECHS1 gene mutations.

DISCUSSION:

A wide phenotypic spectrum is now emerging for *ECHS1*, ranging from lethality in the first months of life to adult patients who may not fulfil all criteria for LD. Urine metabolite levels correlate with clinical severity and specific measurement of 3-hydroxyisobutyryl-carnitine can distinguish between the two disorders.

CONCLUSION:

The presence of *erythro*-2,3-dihydroxy-2-methylbutyrate in urine organic acid analysis in the clinical setting of Leigh Disease should prompt consideration of ECHS1 and HIBCH deficiency.

Poster 15

From Finger Prick to Finger Tip – Phenylalanine Results by Text for Patients with PKU

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INTRODUCTION

Patients with phenylketonuria (PKU) require regular monitoring of their blood phenylalanine (Phe) levels. This sample can be collected at home by finger prick on to a dried blood spot card and posted to the metabolic laboratory. Following a successful pilot study earlier this year, and thanks to collaboration between the laboratory, dietetic and ICT departments, patients can have instant results available on their mobile phones at their finger tips.

INFORMATION FLOW

The dried blood spots are analysed for Phe using tandem mass spectrometry and this analyser is interfaced with the laboratory information system (iLAB). When the results are fully authorised by a scientist, they are automatically sent to an interface server, for matching with the patient information management system (iPIMS). From here a web page is created which is validated by a metabolic dietitian, then sent to the texting server (Defero). This system sends either a 'normal' or 'abnormal' text message to the PKU patient (or parent/guardian if a minor).

TARGET LEVELS

In order to label a Phe result as 'normal' or 'abnormal', target ranges had to be defined for PKU patients of different categories (paediatric, maternal or older adult) and used instead of reference ranges in iLAB.

TEXT MESSAGES

Phe results flagged as 'normal' will be sent a text message containing the numeric value and that no dietary changes are necessary. However, patients with 'abnormal' Phe results will not be given a numeric value but asked to phone the metabolic unit dietitian.

PILOT STUDY

The cohort of patients aged 18 months – 4years were selected for the pilot study (n = 27). For babies less than 18 months all results are phoned in order to give dietary advice and direct support. Up to 4 years blood samples are provided at least weekly. The study commenced in Dec 2014 and by May 2015 we had monitored 1,111 dried blood spot samples.

RESULTS

The results showed that for this group, 37% of Phe levels were 'normal' and this reduced the number of dietetic phone calls by that percentage (411 calls saved). The actual Phe level was slightly reduced: there was an 11.6% variance on levels monitored for 3 months preceding study and 3 months into study. This suggests that there could be improved compliance with diet when results are received in this manner.

CONCLUSION

Due to the success of this pilot study the texting scheme is being offered to all consenting PKU patients when attending metabolic clinic. To date there are over 200 patients enrolled. The percentage of 'normal' results currently stands at approx 60%. Considering that we perform >6,000 Phe tests per annum, and if the majority of patients consent to receiving results by text, the number of dietetic phone calls will be dramatically reduced. More importantly, patients are getting quicker results, compliance with diet potentially may be improved, with the aim for a better patient outcome.

Poster 16

Evaluation of the performance of a revised hypoglycaemia work-up in infants and children

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Hypoglycaemia is one of the more common metabolic emergencies in neonates and childhood and requires prompt diagnosis and management to prevent potentially irreversible brain damage. Collection of critical samples at the time of hypoglycaemia is important to investigate the possible cause. This audit was undertaken to evaluate the performance of a revised hypoglycaemic protocol and to assess the outcome.

All individuals had sufficient investigations performed at the time of the initial episode to identify a probable endocrine and metabolic cause of hypoglycaemia. More than three quarters of the hypoglycaemic work-ups originated from infants and children attending the ED department. Ketotic hypoglycaemia the most common causes, a significant proportion of those tested being rotovirus positive. Approximately 20% presented with hyperinsulinism. These infants had significantly lower plasma cortisol and higher plasma growth hormone levels compared to those with ketotic hypoglycaemia.

Sufficient laboratory information was available within 4 hours (Monday to Friday) or on the next working day) to make a provisional diagnosis compared to more than 200 hours over a similar period one year previously.

Following the introduction of the revised hypoglycaemic work-up, there has been a significant reduction in the time to make a provisional diagnosis, thus enabling ED paediatricians to more effectively manage admissions/discharges. Endocrine investigations need to be interpreted with caution in infants presenting with hyperinsulinism.



Improving pregnancy outcomes

Short-term prediction tool for pre-eclampsia

Pre-eclampsia accounts for 42% of all maternal deaths per year worldwide¹. The current established diagnosis of pre-eclampsia involves blood pressure measurement and determination of protein in urine, the prognostic performance of which is quite poor². As a consequence many women with signs associated with pre-eclampsia are unnecessarily hospitalised for intensive monitoring, resulting in significant additional costs to pregnancy care. There is an unmet medical need for short-term prediction of pre-eclampsia in pregnant women with suspected pre-eclampsia.

The PROGNOSIS study is addressing this unmet need. It is the first clinical study to demonstrate short-term prediction of pre-eclampsia using Roche's fully automated Elecsys® sFlt-1/PIGF serum maternal blood testing in pregnant women with clinical suspicion of pre-eclampsia. The study commenced in December 2010 across 14 countries and 31 sites worldwide.

Dr Manu Vatish, Senior Clinical Fellow & Consultant in Obstetrics, at the, Nuffield Department of Obstetrics & Gynaecology, University of Oxford & the John Radcliffe Hospital, Oxford, who is one of the study investigators, stated that "The Roche sFlt1/PIGF ratio has an extremely high negative predictive value which has the capacity to change the way in which we make our initial assessment of patients, permitting outpatient care and monitoring for those at low risk of the disease whilst focusing our inpatient care on those at highest risk of complications. This has benefits for the mother, the hospital and the clinician".

The PROGNOSIS Study showed that with the Elecsys® sFlt-1/PIGF ratio it is possible to identify patients that are at high risk of developing pre-eclampsia in the next 4 weeks as well as confidently sending home patients that are not going to develop the disease in the next week. The full results of the study were announced at the COGI conference in 2014 and will be published in the Medical Literature shortly.

1. Verlohren S et al. 2010. Am J Obstet Gynecol 202 (161): e1-11
2. Steegers EAP et al. 2010 Lancet 2010; 376: 631-44



Poster 17

Development of a Tandem Mass Spectrometry method for total and free carnitine analysis and comparison of acylcarnitine profiles from patients on ketogenic diets using plasma and dried blood spot assays

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The analysis of plasma and dried blood spot samples for acylcarnitine profiles is an important tool in screening for inborn errors of metabolism, especially disorders of fatty acid metabolism. Other alterations to fatty acid metabolism, in ketosis for example, are also reflected in the patterns of acylcarnitines. The ketogenic diet is a strict diet used in the treatment of intractable epilepsy and in some inborn errors of metabolism including pyruvate dehydrogenase complex deficiency and glucose transporter type 1 deficiency. The principle of the diet is to induce a constant state of ketosis and the use of ketones as the main energy source, which has been shown to improve seizure activity in epileptic patients.

This study was undertaken to develop and validate a tandem mass spectrometry assay to measure acylcarnitines in plasma and assess the effect of the ketogenic diet on acylcarnitine profiles of patients. Acylcarnitines are also analysed in dried blood spots; the presence of long chain acylcarnitines in the red cells found in dried blood spots can make the diagnosis of some fatty acid oxidation defects difficult. This study compared the acylcarnitine profiles in paired plasma and dried blood spot samples collected from patients on, or about to start, the ketogenic diet.

In summary, the development and validation of an assay to measure acylcarnitines in plasma has been successful and provides an additional method, in conjunction with dried blood spot analysis, for screening of metabolic disorders and monitoring of free carnitine. The study of the acylcarnitine profiles from patients on the ketogenic diets showed that free carnitine levels were similar in both plasma and dried blood spot and no patient was found to be deficient in free carnitine. Elevated levels of the ketotic marker hydroxybutyrylcarnitine, were present in most of the patients compliant on the diet, proving that the patients were in a state of ketosis. Tetradecenoyl carnitine, a marker also associated with ketosis, was not elevated in any patient; this is not as reliable a marker as hydroxybutyrylcarnitine for assessing ketosis.

Poster 18

The Validation of an Anti-Müllerian Hormone assay and an investigation into its uses to support a fertility clinic

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INTRODUCTION:

Anti-Müllerian Hormone (AMH) is a peptide hormone involved in sexual differentiation. It is proposed that serum AMH be used as surrogate marker for the Antral Follicle Count (AFC) as a strong correlation is observed. AMH quantitation has a number of proposed diagnostic applications and an increased use in the infertility setting.

OBJECTIVES:

To validate the Roche AMH assay for use on the Roche Cobas e411 platform. This study also involved a correlation study with the AFC measurement on day three of the menstrual cycle and a stability study.

METHODS:

Convenient sampling was used to collect patient samples from the fertility clinic and gynaecology clinic associated with the National Maternity Hospital (NMH). The primary sample was referred to The Doctors Laboratory (MedLab) as routine sampling and sample aliquots were refrigerated or frozen on receipt prior to analysis.

RESULTS:

The bias between the Roche and the Beckman Coulter (MedLab) methods was not clinically significant at clinically relevant ranges (mean bias= -2.51 pmol/L) with a high correlation coefficient.

We identified a high correlation between the serum AMH concentration and the AFC measurement (Roche e411 AMH assay: Correlation coefficient= 0.853, p-value <0.05; Beckman Coulter AMH Gen II assay: Correlation coefficient= 0.824, p-value <0.05). Our data demonstrates that serum samples are stable at 4°C for up to three weeks and one week at 20-25°C. Whole blood samples are estimated to be stable for greater than one week at 4°C.

CONCLUSIONS:

The Roche AMH assay was deemed suitable for routine use in the Biochemistry laboratory with the Cobas e411 platform. Serum AMH appears superior to AFC measurement, with automated assays demonstrating increased reliability to manual methods.

Poster 19

The Alpha-1 Antitrypsin Deficiency National Targeted Detection Programme

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AAT deficiency (AATD) is a hereditary disorder caused by mutations in the SERPINA1 gene, classically presenting with chronic obstructive pulmonary disease (COPD) and/or liver and skin disease. The most common harmful mutation is Z (Glu342Lys), but over 100 other harmful mutations exist. AATD is under-diagnosed and prolonged delays in diagnosis are common despite ATS/ERS guidelines advocating screening all COPD, poorly-controlled asthma and cryptogenic liver disease patients as well as those with necrotising panniculitis and first degree relatives of known AATD patients.

14,500 individuals have been screened to date following ATS/ERS guidelines in the national targeted detection programme which began in 2004. AAT phenotyping is performed by isoelectric focusing and AAT levels are determined by immune turbidimetry. Sequencing of the SERPINA1 gene is performed to identify rare mutations.

We have identified 259 ZZ, 196 SZ, 73 SS, 2058 MZ, 1467 MS, and over 250 individuals with rare phenotypes (e.g. IZ, FZ, IS, Null, M_{malton}). A number of novel SERPINA1 mutations have been identified. Of all samples tested to date 30% carry at least 1 AAT mutation.

Our results illustrate the high prevalence of AATD in Ireland and the success of a targeted approach. We advocate that all COPD patients should be tested for AATD regardless of age and/or smoking status as per ATS/ERS guidelines. The advantages of a diagnosis of AATD include increased lung and liver surveillance, family member testing, smoking cessation, and the consideration of occupational and environmental exposures.

Poster 20

γ -Secretase Cleavage of TNFR1 mediates the segregation of TNF α -induced survival and pro-apoptotic pathways

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BACKGROUND:

The presenilin dependent γ -secretase protease complex (PS/ γ -secretase) performs an important role in regulating receptor-mediated intracellular signalling events, which have a central role in Alzheimer's disease, cancer progression and immune surveillance [1]. Over the past decade a growing number of immune signalling receptors including IL-1R1, IL-1R2, IL-6R, CXCL16, and CD44 have been shown to be PS/ γ -secretase substrates [2].

OBJECTIVE:

We aim to demonstrate that presenilins have a more varied role in regulating immune responses through its γ -secretase cleavage of cytokine receptors and other receptors involved in immune functions such as the TNF superfamily.

STUDY DESIGN:

Utilising Presenilin 1/Presenilin 2 double-deficient immortalised fibroblasts, we study the response of these cells to TNF-induced apoptosis and formation of TNFR1-associated death-induced signalling complexes in response to TNF in the absence of PS/ γ -secretase dependent cleavage.

RESULTS:

In this study, we show that TNFR1 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 and receptor internalization, TNFR1 is cleaved by the γ -secretase protease. We show that PS1 associates with TRAF2 and RIP1, and that PS1 is recruited to the TNFR1 complex in a TRADD-RIP1 dependent manner. We also show that TRAF2 promotes ubiquitination of TNFR1 and PS1. In presenilin-deficient fibroblasts, we demonstrate reduced formation of TNFR1-associated death-inducing signalling complex II and increased resistance to TNF α /cycloheximide-induced apoptosis.

CONCLUSION:

These observations demonstrate that TNFR1 is a novel substrate for TRAF2 ubiquitination and γ -secretase cleavage and suggest that regulated intramembrane proteolysis of TNFR1 may regulate the recruitment of the death domain adaptor proteins to the TNFR1 signalling complexes that determine if TNF induces cell death or survival.

References:

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Poster 21

Very low serum HDL-cholesterol due to malaria? – a case report

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While low HDL-cholesterol is commonly seen in dyslipidaemias characterised by elevated triglyceride levels e.g. diabetes, it is highly unusual to encounter a HDL-cholesterol < 0.2mmol/L in the absence of concurrent markedly elevated triglycerides. Rare cases have been reported in the context of primary disorders of HDL metabolism e.g. Tangier disease, or the use of medications affecting the retinoid-x-receptor transcription pathway e.g. fibrates and thiazolidinediones

We report the case of a 39-year old West African man in whom we identified undetectable HDL at <0.08 mmol/L. His total cholesterol was 2.85 mmol/L and, notably, he had very mildly elevated triglycerides at 2.32 mmol/L. He was admitted with a two-week history of polydipsia, polyuria, weight loss and hyperpyrexia. Dual malarial infection with *Plasmodium ovale* and *falciparum* was identified and attributed to a recent trip to Nigeria. In addition, he was diagnosed with diabetes mellitus with random hyperglycaemia of 39 mmol/L but no ketonaemia. Subsequent investigation revealed an apolipoprotein A1 of 0.38 g/L (1.04-2.02), confirming a true HDL-cholesterol deficit.

On clinical examination he had neither orange tonsils consistent with Tangier disease nor corneal opacification consistent with lecithin-cholesterol acyltransferase deficiency. He was noted to be an avid gym-goer and the possibility of HDL-cholesterol reduction due to anabolic steroids was considered. However, the patient strenuously denied taking any performance-enhancing substances and his sex hormone profile was not indicative of hypothalamic-pituitary-gonadal axis suppression. A surprising correlation between malaria and hypoalphalipoproteinaemia was identified on literature review with a reported mean reduction in HDL-cholesterol of 0.32mmol/L between patients and non-infected controls, raising malaria as a possible major contributing factor to the low HDL.

This case illustrates the need of thinking more broadly about the possible causes of HDL deficiency and highlighting malaria as a potential aetiological factor.

Poster 22

Clinical audit of the genotypic frequencies of Hereditary Haemochromatosis referrals to Cork University Hospital 2009-2012

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INTRODUCTION

Hereditary Haemochromatosis (HH) defines a complex heterogeneous group of autosomal recessive disorders that result in multi organ iron overload with the liver parenchymal cells being primarily affected. Our study concentrated on HFE-related haemochromatosis, the most common cause of HH.

AIMS/BACKGROUND

Clinical expression of HH is variable with the C282Y homozygous genotype representing the largest group. However, even within this group, approximately 75-85% do not develop HH owing predominantly to its varied penetrance. There have been few studies extensively reviewing genotype population frequencies in Ireland to date. Our study aims to assess the frequencies of the various genotypes recorded from referrals to CUH. A further objective is to correlate the different genotypes with biochemical iron overloading to establish any statistically significant variations in altering the percentage Transferrin saturation (TS%) cutoff for iron overload.

METHOD

The audit encompasses a retrospective review of referrals for HH genotype testing to the Clinical Biochemistry Department from the periods August 2009 to December 2012. The referrals were divided into Diagnostic, Predictive and Carrier Status groups as per best practice guidelines. Iron overload was defined into two groups; TS >45% and TS >55%. Data was anonymised and the following variables were recorded on each patient: Ethnicity, Age, Sex, Referrer, TS, Ferritin, Comorbidities (Elevated LFTs, Cardiomyopathy, DM, Arthritis) and HH genotype. Genotyping was performed using fluorescent PCR for HFE mutations p.Cys282Tyr (C282Y), p.His63Asp (H63D) and p.Ser65Cys (S65C). All analyses for the project were conducted using Statistical Analysis System.

RESULTS

A total of 2,511 referrals were included in the study. The predominant age was 35- 65 years (65% of total). Diagnostic referrals accounted for 62% (1,517) of total with GP's making 93% of referrals. The overall genotype frequencies showed C282Y homozygous represented 20% of the overall population (497 patients), compound heterozygotes recorded at 13% (329 patients) and C282Y carriers were seen in just over a quarter of the population (26%). Above 55%, C282Y homozygous patients represent 75% of HH diagnoses. In a cohort of 139 patients with "severe" biochemical overload with TS>45% and Ferritin >1,000, an expected majority were C282Y homozygous (53%). "Normal" patients without a HFE mutation accounted for 20% of these severe iron overloaded patients.

CONCLUSION

This study shows a high carrier rate of C282Y among the population (26%). C282Y specificity rises dramatically above levels of TS>55%. There remains an unexplained high level of the population (20%) with normal genotyping and severe biochemical iron overload. This finding requires further investigation.

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