

PROCEEDINGS OF

THE 30TH ANNUAL CONFERENCE

Of the Association of Clinical
Biochemists In Ireland

0.00 32.00 34.00 36.00 38.00 40.00 42.00 44.00 46.00 48.00 50.00 52.00 54.00 56.00 58.00



HILTON HOTEL
CHARLEMONT PLACE
DUBLIN 2, IRELAND

19th - 20th October, 2007





WELCOME TO ACBI 2007

PROCEEDINGS OF

The 30th Annual Conference

Of the Association of Clinical Biochemists In Ireland

**HILTON HOTEL, CHARLEMONT PLACE
DUBLIN 2, IRELAND**

19th - 20th October, 2007





The ACBI in Ireland and the World

The Association of Clinical Biochemists in Ireland (ACBI) is the national society for Clinical (Bio)chemistry of the Republic of Ireland. The ACBI is a member society of the International Federation of Clinical Chemistry (IFCC) and of the IFCC's "geographical" sub-groups FESCC (Forum of European Societies of Clinical Chemistry) and EC4 (European Communities Confederation of Clinical Chemistry). The ACBI is a sponsoring society of Clinical Chemistry and Laboratory Medicine (formerly European Journal of Clinical Chemistry and Clinical Biochemistry).

The Association works closely on matters of common interest with its sister organizations the Academy of Medical Laboratory Science and the Faculty of Pathology of the Royal College of Physicians of Ireland through joint committees such as the Steering Committee of the Irish External Quality Assessment Scheme (Laboratory Medicine), and the Joint Working Group on Accreditation of Irish Clinical Laboratories. The Association's website is www.acbi.ie

The Association's logo incorporates Celtic symbols of knowledge and of healing, to represent science and medicine. It comprises an abstracted image of water to represent the otherworld well of wisdom, and the spring of healing, and also the cauldron of regeneration.

Also depicted are the hazels of wisdom and inspiration. It was by eating the hazel nuts, which fell into the well, that the salmon of knowledge acquired its wisdom.

The elements of the logo are grouped in threes to echo the triadic motif common in Celtic imagery.

A further characteristic is the openness to interpretation at various levels of meaning. Thus, the lower part echoes a common schematic used in biochemistry to represent molecules migrating in a matrix.





Table of Contents

	page
• Acknowledgements	1
• Welcome to ACBI 2007	2
• Continuing Education	3
• Programme	4
• Speakers' Abstracts	8
• Poster Abstract Index	19
• Poster Abstracts	23





Acknowledgements

The organizing committee for ACBI 2007 gratefully acknowledges the very generous support of the following:

Major Sponsors:

Abbott Diagnostics Division
Beckman Coulter
Brennan & Company
Claymon Laboratories Limited
Cruinn Diagnostics Limited
Olympus Diagnostic Systems
Roche Diagnostics Limited
Randox Laboratories Limited
Siemens Medical Solutions, Diagnostics, Ltd.

Associate Sponsors:

Unitech Limited
Jeol UK Ltd.

Additional Sponsors:

Aalto Bio Reagents Limited
Elga Process Water
Medicon Irl. Ltd.
ScheBo Biotech

The following Major Sponsors have provided significant additional support for the Conference:

Abbott Diagnostics Division
Brennan & Company
Claymon Laboratories Ltd.
Olympus Diagnostic Systems

Céad Míle Fáilte



Welcome to ACBI 2007

We extend a warm welcome to ACBI members, to our distinguished speakers, to our guests, to our ACBI colleagues and to all who attend this conference. We hope that you will enjoy the scientific and social programmes.

For the second year running the conference organising committee is based in the Children's University Hospital, Temple Street. Due to last year's successful running of the conference we return to the Hilton Hotel Charlemont. We hope that visiting delegates will also find some time to extend their stay to enjoy some of the sights and entertainment that Dublin has to offer.

Our scientific programme this year covers renal pathophysiology and the direct role we in the laboratory play in supporting the diagnosis and treatment of renal patients. We will also hear about the latest technologies and therapies in molecular medicine. The session on the 'Highs and Lows of Sugar' considers the medical, biochemical and patients' perspectives on disorders of glucose metabolism.

Following the favourable response to the Case History session in 2006 it was decided to hold a similar format this year. The session will be introduced by a presentation on data interpretation. We hope that the cases presented will encourage interactive discussion.

As a tribute to the late Des Kenny, founder member and past President of ACBI, we are dedicating the final lecture on Friday afternoon to his memory, with a presentation on Quality, a topic to which he showed great commitment throughout his career.

In honour of the late Geraldine Roberts a medal will be awarded to the presenter of the best poster displayed at the conference. This award will be kindly sponsored by her family for ten years. We are happy to see an increased number of posters on display this year and please find the time to read them and discuss with their authors.

We hope that the scientific aspects of the conference will enhance your knowledge and contribute to your on going professional development.

The successful organisation of this conference depends greatly on the generous support of our sponsors. We extend a special welcome to the delegates of the conference sponsors.

Finally we would like to thank the members of the ACBI Council for their continuing support and encouragement.

**Deirdre Deverell (Chairperson), Maire Oakley (Conference Secretary),
Anne O Shea, Richard Walsh, Philip Mayne**

ACBI 2007 Conference Committee.



Continuing Education

The Royal Colleges

ACBI 2007 has been approved for CME by the Royal College of Physicians of Ireland (RCPI) and for CPD by the Royal College of Pathologists (RCPATH). All medical Royal Colleges in Ireland and the UK have agreed to recognise each other's approval of events.

Medical staff and clinical biochemists who have completed training and are in career grade posts and have registered for CME or CPD with one of the Royal Colleges are entitled to receive CME or CPD credits.

CME approval: Fri 20th Oct = 5 credits, Sat 21st Oct = 7 credits

CPD approval: Max 11 credits for the two day meeting

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

Academy of Medical Laboratory Science

ACBI 2007 has been approved by the Academy of Medical Laboratory Science (AMLS) for the award of CPEP points. Five CPEP points will be awarded for each half-day attended or twenty CPEP points for attendance at the full conference. In order to receive these points, an AMLS member must sign the AMLS attendance register and be issued with a certificate of attendance by the meeting organiser.

Evaluation of meeting

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



Friday 19th October 2007 (Morning)

08:30

Registration

Opening Ceremony

09:30 - 9:45

ACBI President's Address
Dr. Alan Balfe

09:45 - 10:15

Opening Lecture by Guest Speaker
Ms. Mary Harney TD, Minister for Health and Children

Session 1

Renal Pathophysiology

Chairperson: Dr. Ophelia Blake, St. James's Hospital, Dublin

10:15 - 11:00

Chronic Kidney Disease Initiatives: Implications for the Laboratories
Dr. Damian Fogarty, Belfast City Hospital

11:00 - 11:30

Tea/Coffee Break

11:30 - 12:15

Clinical Biochemistry and Renal Transplantation
Dr. Atif Awan, Children's University Hospital, Dublin

12:15 - 13:00

eGFR Quality Assurance: Methodological Disparity
Mr. Finlay MacKenzie, UK NEQAS Birmingham

13:00 - 14:15

Lunch Break



Programme

Friday 19th October 2007 (Afternoon)

Session 2

Molecular Medicine

Chairperson: Dr. Alan Balfe, St. James's Hospital, Dublin

14:15 - 15:00

Genetic Testing as a Diagnostic Tool

Professor Andrew Green, National Centre for Medical Genetics, Crumlin

15:00 - 15:45

Targeted Molecular Therapies

Professor John Crown, St. Vincent's University Hospital, Dublin

15:45 - 16:15

Tea / Coffee Break

16:15 - 17:00

Des Kenny Tribute Lecture

Quality: What is it and why does it matter?

Dr. Graham Beastall, NHS Greater Glasgow & Clyde; President ACB

ANNUAL GENERAL MEETING

17:15 - 18:00

ACBI Members only

19:00 - 20:00

Pre Dinner Drinks Reception

20:00 - 24:00

Annual Dinner

Musical Entertainment by Cormac Kenevey and the Velvet Lounge Band



Saturday 20th October 2007

Session 3

'The Highs and Lows of Sugar'

Chairperson: Dr. Orla Maguire, St. Vincent's University Hospital, Dublin

9:30 - 10:15

Biochemistry and Diabetes - A Special Relationship
Dr. Ned Barrett, Mid-Western Regional Hospital

10:15 - 11:00

Investigation of Hypoglycaemia in Childhood
Dr. Jim Bonham, Sheffield Children's Hospital

11:00 - 11:30

Tea / Coffee Break

11:30 - 12:15

Customised New Molecules for the Treatment of Diabetes
Professor John Nolan, Metabolic Research Unit, St. James's Hospital and TCD

12:15 - 13:00

Living with Diabetes - the Patients' Perspective
*Ms Anna Clarke, Health Promotion and Research Manager,
Diabetes Federation of Ireland*

13:00 - 14:15

Lunch Break

Session 4

Data Interpretation and Case Histories

Chairperson: Professor Philip Mayne, Children's University Hospital, Temple St., Dublin

14:15 - 14:45

Poster Presentations for Geraldine Roberts Award
Judges Panel: Dr N Barrett, Ms E Duly, Ms H Moore

14:45 - 15:15

What Do These Results Mean?
Professor Philip Mayne, Children's University Hospital, Dublin

15:15 - 15:45

Case History 1
Tim Lang, Royal Victoria Hospital, Belfast

15:45 - 16:15

Tea/Coffee Break

16:15 - 16:45

Case History 2
Mary Stapleton, Cork University Hospital

16:45 - 17:15

Case History 3
Paula O Shea, Beaumont Hospital

17:15

Presentation of Geraldine Roberts Memorial Medal
Brian Sheridan, Royal Victoria Hospital, Belfast

17:30

Closing Remarks of ACBI 2007
Deirdre Deverell, Chairperson ACBI 2007 Conference Committee



Speakers' Abstracts & Biography Session 1

'RENAL PATHOPHYSIOLOGY'

Chronic Kidney Disease Initiatives: Implications for the Laboratories

Damian G. Fogarty, MD, FRCP. *Belfast City Hospital & Queen's University Belfast, Northern Ireland. d.fogarty@qub.ac.uk*

ABSTRACT

Chronic Kidney Disease (CKD) can manifest as either reduced kidney function or urinary abnormalities or a combination of both. Estimated glomerular filtration rate (eGFR) has emerged as the major basis for a 5-stage CKD classification [1]. Patients with an eGFR < 60ml/min/1.73m² over at least 3 months are deemed as CKD stage 3, 4 or 5 and are the focus of the UK General Practice CKD quality indicators [2]. Various laboratory based surveys in the UK estimate that 3-5% of patients sampled have CKD of this degree. It is important to recognise that this is an underestimate as there are no local population-based studies of true CKD prevalence.

With an eGFR of 60ml/min or greater, the diagnosis of early CKD requires the presence of other kidney damage e.g. persistent proteinuria/albuminuria, persistent microscopic haematuria or structural kidney disease. Estimates suggest that the prevalence of microalbuminuria could be as high as 7-10% depending on gender and race [3]. As well as being markers of renal risk these CKD indicators signify increased cardiovascular risk and have thus been suggested as screening tools. Whilst we await this evidence base to improve laboratories must contend with services for the aging population with increased prevalence of diabetes, hypertension and kidney disease.

1. Levey AS, Eckardt K-U, Tsukamoto Y et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2005; 67: 2089-2100
2. Doran T, Fullwood C, Gravelle H et al. Pay-for-performance programs in family practices in the United Kingdom. *N Engl J Med*. 2006 27;355(4):375-84
3. Tillin T, Forouhi N, McKeigue P, Chaturvedi N. Microalbuminuria and coronary heart disease risk in an ethnically diverse UK population: a prospective cohort study. *J Am Soc Nephrol* 2005;16: 3702-3710

BIOGRAPHY

Dr Damian Fogarty is Consultant Nephrologist and Senior Lecturer in the Regional Nephrology Unit, Belfast City Hospital and Queen's University Belfast. He trained in Belfast before moving to Harvard University, Boston as a Fulbright fellow at the Joslin Diabetes Centre. On return he took up his first consultant post at Antrim Hospital. He moved to his current post in 2002.

He has clinical and research interests in diabetic nephropathy and the broader epidemiology of chronic kidney disease. He has published significant papers in these areas and co-ordinated the guidelines for CKD management in Northern Ireland. He has advised the Department of Health on hypertension, diabetes and kidney disease. He represents the region on the UK Renal Registry Committee and is a founding member of the UK Renal Association Epidemiology subgroup.



Speakers' Abstracts & Biography

Clinical Biochemistry and Renal Transplantation

Dr Atif Awan

*Department of Nephro-urology & Transplantation,
Children's University Hospital, Temple Street, Dublin 1.*

ABSTRACT

Children with renal failure have specific requirements in terms of growth and development. The paediatric nephrology programme provides dialysis facilities for infants and children of all age with a view to successful transplantation once over the age of 2 years. The work is labour intensive and requires a multidisciplinary team approach to individual patients. To achieve all the best practice parameters biochemical analysis play a pivotal role in keeping the children healthy before, during and after transplantation.

BIOGRAPHY

Atif Awan graduated in Medicine in Pakistan. His post graduate training took place in UK and Ireland. He worked as a pediatric nephrologist in the Royal Manchester Children's Hospital in Pendlebury before coming to the Children's University Hospital, Temple St in 1999. His speciality is pediatric dialysis and transplantation.

He set up the National Paediatric Haemodialysis Service in 2000 and in 2003 the National Paediatric Transplant Programme moved from Beaumont Hospital to the Children's University Hospital. There have been 32 transplant operations performed.



Speakers' Abstracts & Biography

eGFR Quality Assurance: Methodological Disparity

Mr. Finlay MacKenzie

UK NEQAS Birmingham

ABSTRACT

The Department of Health (in England) recommended implementation of routine eGFR reporting by all NHS clinical biochemistry laboratories by 1st April 2006. This was scheduled to fit in with the Quality Outcome Framework (QOF) for General Practitioners, which came into effect at the same time. An Advisory Group was set up and one of the issues that was addressed was how to best harmonise the reporting of eGFR, given the different equations in use and the differences seen in laboratory creatinine assays.

The UK NEQAS involvement was to be two-fold: an initial data gathering and mathematical analysis followed by an ongoing, but strictly necessary, monitoring process. This would assess the impact of the new variables and ensure that the equations remained valid over time. This second point is crucial. Because the creatinine results were to be directly influencing treatment stratifications, it was anticipated that laboratories would want to move to better methodologies as they became available.

A series of slope and intercept adjusters was produced which could be used as a short term measure to allow us, the laboratory community, to buy some time to get better creatinine methods in place. Highlighting deficiencies was the easy part. The difficulty was, and still is, in trying to persuade laboratories that the traditional Jaffe methods were no longer fit for purpose. Despite the financial ramifications, a move to specific and sensitive methods is the only way forward. Calibration, per se, is not the issue.

The UK NEQAS for GFR estimates is a specialised scheme which can thoroughly probe this area in a way that a 'general chemistry' EQA scheme cannot. It continues to address issues of accuracy, analytical interferences and probes the effect of the creatinine results on a range of clinical scenarios.

BIOGRAPHY

Finlay MacKenzie began his career in Clinical Biochemistry working at Queen Charlotte's Maternity Hospital. During this time he attained an MSc in Clinical Biochemistry from the Faculty of Medicine at the University of London. Staying in London, he then worked at another Teaching Hospital, (St. George's) before entering the speciality of EQA at the Wolfson Research Laboratories, Birmingham. Finlay has contributed widely to the output of this, the largest EQA provider in Clinical Biochemistry, for over twenty years.

His first position in EQA was as Scheme Manager of the UK NEQAS for Thyroid Hormones (he is now the Organiser), but over the years has widened his interest into many other areas of Clinical Biochemistry EQA. He is a Deputy Director of the Wolfson EQA Laboratory.

He has been responsible for much of the computing innovations over the years for both his own and other centres. He says his greatest achievement was the introduction of the 'ABC of EQA', which is a statistical and graphical approach to the data processing and reporting of EQA data and which is built on good scheme design. Finlay was on the Department of Health's [UK Government] expert group for eGFR and looking at 'standardisation' of creatinine. Recently, Finlay has made a name for himself by robustly challenging the entrenched practice in laboratories of 'fudging' results. He speaks regularly at a range of events from UK NEQAS Roadshows, Company User-Groups, Scientific Meetings (both in the UK and abroad) as well as having a commitment to post-grad and under-grad teaching at Birmingham University.



Speakers' Abstracts & Biography Session 2

'MOLECULAR MEDICINE'

Genetic Testing as a Diagnostic Tool

Professor Andrew Green

National Centre for Medical Genetics, Crumlin, andrew.green@olhsc.ie

ABSTRACT

The use of genetic technology to give accurate diagnosis for a wide range of genetic disorders is undoubtedly a great advance in healthcare. The earliest clinical use of genetic technology was cytogenetic analysis to diagnose constitutional chromosome disorders, and later to analyse chromosome anomalies in haematological malignancies. DNA technology then came on stream, and is used to aid in diagnosis of many single gene disorders, such as cystic fibrosis, Huntington's disease and muscular dystrophy. Such technology can now also be used to provide predictive tests for healthy people who have a single gene disorder such as Huntington's disease in their family.

Parallel with the development of new genetic technologies has been the development of high quality diagnostic genetic laboratories, with critical masses of expertise, multidisciplinary teams, EQA and external accreditation.

With the vast numbers of disease genes now being described, introducing new gene tests may at first sight seem simple, but in fact, needs to be assessed very carefully. The decision to introduce a new genetic test needs to be weighed up according to 4 components, analytical validity, clinical validity, clinical utility, and the ethical legal and social implications of introducing the test.

The assessment of new gene tests is difficult, even when such tests are for rare but fully penetrant single gene disorders. The introduction of such tests, when the test is studying one of many genes which may contribute to a polygenic disorder, is even more fraught. Such potential polygene tests include thrombophilia gene polymorphisms, low penetrance cancer susceptibility genes, and genetic risk factors for vascular disease.

With high throughput genome sequencing, and high density genomic arrays, vast amounts of genetic information on an individual can be generated. However, clinically useful interpretation of such data will be even more of a challenge than the technology.

BIOGRAPHY

Andrew Green is a UCD Medical Graduate, and did a PhD in Cambridge UK with Sydney Brenner (Nobel Laureate 2002), where he also trained in clinical genetics. He has been Director of the National Centre for Medical Genetics since 1997, where he is a consultant in clinical genetics in both Our Lady's Hospital Crumlin and the Childrens University Hospital, Temple Street, and is also Professor of Medical Genetics in UCD. He has been involved in a wide range of research programmes, including the genetics of motor neuron disease, and more recently is a member of the Autism Genome Project, which recently got a €5 million HRB grant. He also has an interest in ethics and genetics and was a member of the Commission on Assisted Human Reproduction, and a member of the Irish Council for Bioethics.



Speakers' Abstracts & Biography

Molecularly Targeted Therapy in Cancer: Smartbombs v Blunderbusses

Professor John Crown

St. Vincent's University Hospital, Dublin

ABSTRACT

There has been a dramatic change in the drug treatment of cancer in recent years. Increasing knowledge of the molecular basis of malignancy has resulted in the identification of numerous "druggable" molecular targets. As a result, molecular therapeutics have entered the mainstream, and are routinely used in the treatment of carcinoma of the breast, bowel, kidney, lung, upper digestive tract, liver, haematopoietic system, and in malignant melanoma. The two drugs which have had the greatest impact to-date have been Imatinib which has transformed the treatment of chronic myeloid leukaemia and Trastuzumab (Herceptin) which has been shown to have substantial survival benefit for patients with Her2 over-expressing breast cancer at all stages of their disease.

The availability of two molecular therapies (Bevacizumab and Cetuximab) for the treatment of patients with metastatic colorectal cancer, has also contributed very meaningfully to the dramatic improvement in the therapy of this disease in recent years.

This molecular revolution represents the convergence of the clinical and biological research projects into one seamless translational cancer research enterprise which is proceeding at breathtaking pace around the world.

Ireland has had a meaningful role in this process and the Irish Clinical Oncology Research Group (ICORG) has facilitated the enrolment of many hundreds of Irish patients on trials with molecularly targeted treatments.

BIOGRAPHY

John Crown is a Consultant Medical Oncologist with St. Vincent's University Hospital and St. Luke's Hospital in Dublin, Ireland. In November 2003, he was awarded the Thomas Baldwin Research Chair in Translational Cancer Research from Dublin City University and in December 2004 was awarded the Newman Clinical Research Professorship in the School of Medicine of University College Dublin.

Professor Crown is a founding member and leader of many organizations that include the Irish Clinical Oncology Research Group, the Anglo-Celtic Oncology Group, the European Breast Cancer Dose Intensity Study, and the Irish Society of Medical Oncology. His other memberships include ASCO, AACR, and ESMO. Professor Crown chairs the Breast Committee of the Irish Clinical Oncology Research Group (ICORG).

Professor Crown received his medical training at the University College Dublin and the State University of New York. He received his postdoctoral training on both sides of the Atlantic. Professor Crown went on to complete his fellowship training in oncology at Mount Sinai Medical Centre and in haematology/oncology at Memorial Sloan Kettering Cancer Centre. He served as assistant professor at Cornell University Medical College before joining St. Vincent's University Hospital in 1993.



Speakers' Abstracts & Biography

Quality: What Is It and Why Does It Matter? Des Kenny Tribute Lecture

Graham H Beastall

NHS Greater Glasgow & Clyde; President ACB

ABSTRACT

Quality, like beauty, is in the eye of the beholder. This controversial statement serves to demonstrate that the definition of a quality laboratory medicine service will differ depending on whether the 'beholder' is an international standards organisation, a laboratory medicine professional, a user of the service or a patient.

We have an impressive array of standards and tools for defining and measuring quality within the laboratory and it has become routine for us to require quality measures for the overall service, for individual components of that service and for the staff that deliver that service. There can be no doubt that by these measures the quality of UK and Irish laboratory medicine services has improved steadily over the past twenty years and that this has been 'a good thing' for the user and the patient.

However, each additional further gain in quality within the laboratory is harder to achieve and there is a view amongst some professionals that the introspective pursuit of quality for quality's sake has deflected our attention from our real role - the provision of a service where the quality is fit for purpose. To better understand that purpose we need to appreciate what the user and the patient expect of a quality service. In an era of patient-centred care we ignore these factors at our peril.

This largely philosophical lecture will aim to stimulate an active debate on the wider aspects of 'quality matters' - and thereby continue the legacy of Des Kenny.

BIOGRAPHY

Dr Graham Beastall is Consultant Clinical Scientist and Clinical Lead for the multi-site network Department of Clinical Biochemistry in North Glasgow, Scotland. He has published more than 170 peer-reviewed articles in the scientific literature. His 'first love' as a specialty area was biochemical endocrinology but more recently he has embraced evidence-based medicine and best laboratory practice in primary care.

Graham has held several representative roles including Secretary of the European Communities Confederation of Clinical Chemistry and Laboratory Medicine (EC4); Vice President of the Royal College of Pathologists (RCPATH); Chairman and currently President of the Association for Clinical Biochemistry (ACB).

Graham has received a number of awards including Fellowship of the Royal College of Physicians and Surgeons of Glasgow; the ACB Foundation Award and the EC4 Distinguished Officer Award. In the June 2007 Queens Birthday Honours Graham was made a Commander of the Order of the British Empire (CBE) for services to medicine.

Graham became close friends with Des Kenny as a result of collaboration on EC4 and other matters over many years. He is honoured to have been asked to deliver the Des Kenny Tribute Lecture.



Speakers' Abstracts & Biography Session 3

'THE HIGHS AND LOWS OF SUGAR'

Biochemistry and Diabetes - A Special Relationship

Dr. Ned Barrett

Mid-Western Regional Hospital, Limerick

ABSTRACT

On 21st December 2006, the United Nations General Assembly passed a landmark Resolution recognising the global threat of the diabetes epidemic. The Resolution calls on all Member States to develop national policies for the prevention, treatment and care of diabetes.

Diabetes is diagnosed and managed using biochemical measurements. Coincidentally, the first biochemists to be employed in a British hospital were appointed in 1921 in the months before the discovery of insulin by Banting and Best in Toronto, Canada. In the decades that followed, biochemistry played a crucial role in enhancing our understanding of diabetes, its causes, pathology, treatment, management and complications.

The development and growth of biochemistry in the twentieth century has provided us with a clear and comprehensive understanding of how insulin is synthesised, secreted and metabolised. We have a better understanding of the mechanism of action of insulin, its role in metabolic regulation and how its production can be affected by autoimmune disease and how resistance to its actions can develop. We know the molecular structure of insulin and can synthesise it using advanced biotechnology. We can alter and modify the structure of insulin for therapeutic benefit. A variety of hypoglycaemic and anti-hyperglycaemic drugs have been used to manage diabetes. We have a greater understanding of the insulin receptor and the intracellular processes that result in the biological response.

Fifty years ago, Berson and Yalow developed the immunological assay of insulin. This new technique was crucial to the development of endocrinology as a specialty and brought about a revolution in medical and laboratory practice.

Clinical trials such as the Diabetes Control and Complications Trial have provided clear and unequivocal evidence of the damaging effects of chronic hyperglycaemia. The measurement of haemoglobin A1c is almost universally used to assess the adequacy of glycaemic control of diabetes. Difficulties in achieving the international standardisation of the haemoglobin A1c assay have provided important and painful lessons for the clinical biochemistry and diabetes community.

BIOGRAPHY

Dr. Ned Barrett B.Sc., M.Sc., Ph.D., EurClinChem, is Consultant Biochemist at the Mid-Western Regional Hospital in Limerick. He was appointed to this new position in 2005.

Dr. Barrett is a graduate of University College, Cork and Trinity College Dublin. He was awarded a Diploma in Health Service Management by the Institute of Public Administration. He is Adjunct Senior Lecturer of Biochemistry at the University of Limerick.

His special interests include diabetes and endocrinology. He is a member of the Health Service Executive's Expert Advisory Group on Diabetes and is Chairman of the Steering Committee of the Irish External Quality Assessment Scheme for Laboratory Medicine (IEQAS).



Speakers' Abstracts & Biography

The Investigation of Hypoglycaemia in Childhood

J R Bonham

*Department of Clinical Chemistry, Sheffield Children's Hospital
NHS Foundation Trust, Sheffield, S10 2TH, United Kingdom*

ABSTRACT

In newborns, the brain represents 10-11% of the total body weight, however, it accounts for approximately 50% of resting energy consumption and while neurones can adapt to the use of alternative fuels including ketone bodies and lactate, glucose remains its most important energy source. As a result, episodic or chronic hypoglycaemia and the resulting neuroglycopenia can impair brain development and cause neuronal damage resulting in lasting neurological impairment. Consequently, the prompt and effective recognition, investigation and treatment of hypoglycaemia in childhood are crucially important if developmental problems are to be avoided.

This presentation will classify the causes of hypoglycaemia during childhood from a laboratory and clinical perspective and will describe and review the guidelines currently in use for its investigation. It will emphasise the logistic requirements and the practical pitfalls commonly encountered when attempting to document hypoglycaemia and investigate its cause. Recommendations will be made to ensure the effective organisation of testing. Reference will also be made to the recent work on glucose transporter defects and the identification of clinically important neuroglycopenia.

BIOGRAPHY

Dr Bonham began working in paediatric clinical biochemistry in 1976 at Newcastle and later moved to Manchester. He has been at Sheffield since 1988 where he is currently Clinical Director for Diagnostics and R&D Director for the Trust. He chairs the Paediatric scientific advisory group of NEQAS and is closely involved with the European EQA provider ERNDIM as a scheme organiser and as a member of its scientific advisory board. He also leads the stakeholder alliance MetBioNet which seeks to establish guidelines for the laboratory investigation of metabolic disease and co-ordinates training for scientists and technical staff working in this area.



Speakers' Abstracts & Biography

Customised New Molecules for the Treatment of Diabetes

John J Nolan

Metabolic Research Unit, St James's Hospital, Trinity College Dublin, Ireland

ABSTRACT

Diabetes mellitus is one of the leading chronic diseases. The prevalence of Type 2 diabetes continues to increase rapidly, driven by the epidemic increase in obesity. Type 1 diabetes is also increasing, though much more slowly, and for reasons that are not completely understood. While the onset of Type 2 diabetes can be prevented or at least delayed by lifestyle intervention and medication, a range of strategies to prevent Type 1 diabetes have been unsuccessful to date. Secondary prevention is the core of clinical diabetes care.

The pharmacological treatment of diabetes has changed significantly in the past ten years. New compounds have been developed to treat both Type 1 and Type 2 diabetes. This presentation will address two main areas:

1. The new analogue insulin molecules, that have been designed, using principles of biochemistry and physical chemistry, to be either more rapidly acting than human insulin, or much more long-acting than human insulin.
2. The range of new orally active medications or non-insulin injectable agents for the treatment of Type 2 diabetes.

The analogue insulins have made it possible to reproduce more closely the kinetics of endogenous insulin action for periods of fasting and for meals. The main advantage to patients of these new insulins has been a significant reduction in the incidence of unwanted hypoglycaemia.

The new agents for Type 2 diabetes include the glitazone, and more recently non-glitazone agonists of PPAR γ - which act as insulin sensitizers. Also newly developed are a series of compounds that act on the GLP-1 axis between gut and CNS. Native GLP-1 has only a fleeting half-life, thus the emphasis has been on developing either long-acting analogues of GLP-1 or prolonging the natural half-life with inhibitors of the enzyme DPP-4.

In this presentation, the structure-function relationships between these new compounds will be outlined, and their place in current and future treatment of diabetes will be discussed.

BIOGRAPHY

Professor John Nolan, physician (Endocrinology and Metabolism), Biochemistry; Trinity College Dublin. Head of Metabolic Research Unit, St James's Hospital, Dublin. Chair: Postgraduate Education Committee, and Executive member, European Association for the Study of Diabetes (EASD), member of American Diabetes Association, The Endocrine Society, European Group for the study of Insulin Resistance. Research interests: diabetes, obesity, insulin resistance, exercise.



Speakers' Abstracts & Biography

Living with Diabetes - the Patients' Perspective

Ms Anna Clarke

Health Promotion and Research Manager, Diabetes Federation of Ireland

ABSTRACT

This is a presentation contrasting stories of the lives of 2 young men diagnosed in their teens with diabetes and now both in their 30s. The stories highlight the individual nature of diabetes and the impact it can have on all aspects of life.

BIOGRAPHY

Anna Clarke is Health Promotion and Research Manager with the Diabetes Federation of Ireland. She has worked as a diabetes nurse specialist setting up the first private diabetes education service in Ireland. As a consultant nurse, she facilitated the Diabetes Service Development Group and compiled the report "Diabetes Care: Securing the Future". She is currently undertaking a PhD with the focus of the research on beliefs and behaviors of people newly diagnosed with type 2 diabetes.

Anna Clarke is currently working as a health promotion and research manager. The focus of the position is

1. to raise awareness of diabetes in the community, workplace and healthcare settings
2. to develop strategies for early detection of diabetes
3. to highlight the risk factors for type 2 diabetes and promote preventative strategies
4. to promote improved access to services for people diagnosed with diabetes
5. to facilitate better understanding from a patient perspective of daily living with diabetes
6. to improve support services for people effected by diabetes and reduce discrimination

The position brings her into daily contact with the main problems and issues faced by people with diabetes. It is this, combined with her understanding of the Irish healthcare system that has resulted in her acceptance by Irish people with diabetes as their advocate at all levels of negotiation and public awareness.



Speakers' Abstracts & Biography Session 4

'CASE HISTORIES'

Data Interpretation: What Do These Results Mean?

Professor Philip Mayne

Children's University Hospital, Temple St., Dublin

ABSTRACT

As clinical biochemistry laboratories become even more busy, scientists are spending even less time reviewing and interpreting biochemical data. Although it is the procedure to telephone abnormal results, scant regard is often given to their interpretation, once the appropriate analytical checks have been performed. Much information can be derived from the most basic biochemical results without recourse to more sophisticated tests. This session, building on a similar session at last year's ACBI conference at which Dr Gordon Challand presented, will explore how reviewing minimal data sets can alter the differential diagnosis and assist in patient management.

This is an interactive session, so participants hiding in the back rows might be asked for the comments!

BIOGRAPHY

Philip D Mayne MD, MSc (Lond), FRCPI, FRCPath, FFPATH (RCPI) is a Consultant Paediatric Chemical Pathologist at the Children's University Hospital, Temple Street, Our Lady's Children's Hospital, Crumlin and the Rotunda Hospital, director of the National Newborn Screening Laboratory and Associate Professor in Biochemistry in the Department of Molecular and Cellular Therapeutics, Royal College of Surgeons in Ireland.

Professor Mayne trained in general medicine in Dublin before undergoing specialist training in chemical pathology in London. He held a number of senior lecturer/honorary consultant posts in London teaching hospitals before returning to Dublin to take up his present post in paediatric chemical pathology. He has published extensively on general and paediatric clinical biochemistry and co-authored a textbook and a number of chapters.



Poster Abstract Index

1. **Evaluation of the Olympus AU3000I Immunoassay System for Serum Leuteinising Hormone and Follicle Stimulating Hormone**
Cundick J, Gamble R, Leslie H, Sheridan B.
Endocrine Laboratory, Department of Clinical Biochemistry, Royal Victoria Hospital, Belfast, Northern Ireland.
2. **Evaluation of the Olympus AU3000I Immunoassay System for Serum Free Thyroxine and Thyroid Stimulating Hormone**
Cundick J, Gamble R, Leslie H, Sheridan B.
Endocrine Laboratory, Department of Clinical Biochemistry, Royal Victoria Hospital, Belfast, Northern Ireland.
3. **Measurement of Urinary Free Cortisol by Abbott ARCHITECT and determination of reference ranges for 24 hour urinary free cortisol and for early morning urine samples cortisol:creatinine ratio.**
Kilpatrick KWE, Brown C, Leslie H, Magill A, Cundick JF, Young IS, Sheridan B.
Regional Endocrine Laboratory, Royal Group of Hospitals, Belfast Health and Social Care Trust.
4. **Chronic kidney disease and its effect on bone turnover in an elderly outpatient population.**
Healy MJ¹, Cronin H², Brewer L², Cox G¹, Walsh JB², Crowley VEF¹, Casey MC².
¹Biochemistry Department, St. James's Hospital, Dublin 8 and ²Mercer's Institute for Research on Ageing, St. James's Hospital, Dublin 8.
5. **Comparison of Alternative Methods of Determining Plasma Transferrin Saturation for the Biochemical Assessment of Iron Overload**
Balfe A, MacNamara B, Crowley V.
Biochemistry Dept, LabMed Directorate, St. James's Hospital, Dublin 8
6. **Does 'Normal' Fasting Glucose Out-Rule Glucose Abnormalities.**
McGing P¹, Al-Agha R², Wright E¹, Kinsley B², Kyne F¹.
¹Biochemistry Department and ²Department of Diabetes and Endocrinology Mater Misericordiae University Hospital, Eccles Street, Dublin 7.
7. **Interference with Lactate Measurement in a case of Ethylene Glycol Poisoning.**
McGing P¹, Dillon-Murphy R¹, Phelan D², Colreavy F², Marsh B², Maguire S¹, Collier J¹.
¹Department of Biochemistry and ²Department of Intensive Care Medicine Mater Misericordiae University Hospital, Eccles Street, Dublin 7.
8. **Aetiology of acute hypoglycaemia: Re-audit of procedures for diagnosis.**
Lang T¹, Cardy D¹, Carson D², Leslie H¹, Loughrey CM¹, Sheridan B¹.
¹Department of Clinical Biochemistry, ²Department of Paediatrics, Belfast Health and Social Care Trust, Belfast.



Poster Abstract Index

9. **Audit of Biochemical Investigations in the Management of Obstetric Cholestasis**
Costa J¹, Lang TF², Hunter A¹
¹Department of Obstetrics and Gynaecology and ²Department of Clinical Biochemistry, Belfast Health and Social Care Trust, Belfast

10. **A case of Nephrotic Syndrome from Childhood to Adulthood**
O'Keane M, Collier G, Cunningham SK.
Biochemistry Department, St. Vincent's University Hospital, Dublin

11. **A Comparative Study between Measured Creatinine Clearance and eGFR assessed by MDRD Formula in different cohorts of Individuals**
Collier G, Reece R, Cunningham SK.
Biochemistry Department, St. Vincent's University Hospital, Dublin.

12. **Glucose Tolerance Testing in Pregnancy.**
O'Kelly RA, Kinsley BT.
Coombe Women's Hospital, Dublin 8.

13. **Painting with Numbers - Workload Analysis across Pathology**
Lanigan O.
The Laboratories, Mater Misericordiae University Hospital, Dublin 7

14. **Negative LDL Cholesterol Estimated using the Friedewald Equation.**
Maguire OC¹, Mc Carthy D², Cunningham SK¹.
¹Department of Biochemistry and ²Department of Haematology, St Vincent's University Hospital, Dublin.

15. **Investigation into causes of interference in the Roche E170 female testosterone assay**
Joyce C, Stapleton MT, O'Mullane J
Biochemistry Department, Cork University Hospital

16. **Clinical and Biochemical Characteristics of Moderate-Severe Hypercalcaemia in a Large Dublin Teaching Hospital**
Lim S, Srinivasan S, Gannon P, Crowley VEF
Biochemistry Department, St James's Hospital, Dublin 8



Poster Abstract Index

17. **Variant Maple Syrup Urine Disease (MSUD) in Three Siblings.**
O'Shea A¹, O'Grady L¹, Treacy EP², Sandona N², Mayne PD¹
¹Biochemistry Department and ²National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple Street, Dublin 1
18. **Development of a Tandem Mass Spectrometry Method for Monitoring Plasma Glutaric Acid and 3-Hydroxyglutaric Acid in Patients with Glutaric Aciduria Type I**
Finnegan N¹, Fitzsimons P¹, Monavari A², Treacy EP², Mayne PD¹.
¹Department of Biochemistry and ²National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple Street, Dublin 1
19. **Clinical, Biochemical and Therapeutic Experience of Pyrroline-5-Carboxylate Dehydrogenase Deficiency (Hyperprolinemia Type II) in Ireland.**
Deverell D¹, Murphy A M², Walsh R¹, Hendroff U³, Treacy EP², Mayne PD¹
¹Department of Biochemistry and ²National Centre for Inherited Metabolic Disorders, ³Department of Clinical Nutrition and Dietetics, Children's University Hospital, Temple Street, Dublin 1
20. **Evaluation of capillary point-of-care results of electrolytes and glucose compared with laboratory analysis in a cohort of premature neonates.**
Corcoran A, Bruen C, Fitzgibbon M.
Department of Clinical Biochemistry, University Hospital Galway, Ireland.
21. **Vitamin D Status in a Healthy Female Population.**
Lardner E, Wilson S, NiChadhain N, Griffin D, Grimes H, Mulkerrin E, Fitzgibbon M.
Department of Clinical Biochemistry, University Hospital Galway, Ireland.
22. **Diagnostic Output of Skin Biopsies in Inherited Metabolic Disorders.**
Pitan C¹, Crushell E¹, Mayne P², O'Neill C², Devaney D², Monavari A¹, Treacy EP¹, Olpin S³, Murphy AM¹
¹The National Centre for Inherited Metabolic Disorders (NCIMDs), ²Department of Pathology, Children's University Hospital, Temple Street Dublin, Ireland. ³Department of Clinical Chemistry, Sheffield Children's Hospital, Sheffield, United Kingdom



Title: Evaluation of the Olympus AU3000I Immunoassay System for Serum Leuteinising Hormone and Follicle Stimulating Hormone

Authors: Cundick J, Gamble R, Leslie H, Sheridan B.

Address: Endocrine Laboratory, Department of Clinical Biochemistry, Royal Victoria Hospital, Belfast, Northern Ireland.

Email: jennifer.cundick@bll.n-i.nhs.uk

INTRODUCTION

New Olympus assays for serum luteinising hormone (LH) and follicle stimulating hormone (FSH) on the AU3000i analyser were evaluated in terms of imprecision, sensitivity, and comparison with results from PerkinElmer® AutoDELFIA and results from samples supplied by UKNEQAS (Edinburgh, UK).

IMPRECISION/SENSITIVITY

For LH, 8 serum pools (range 0.42-52U/L) were assayed on 10 occasions and the CVs ranged from 4.7-2.8%. The CV of the pool with the lowest concentration (0.42U/L) was 4.7% and therefore functional sensitivity must be significantly less than this value. For FSH, 8 serum pools (range 0.75-144U/L) were assayed on 10 occasions and the CVs ranged from 6.4-4.5%. The CV of the pool with the lowest concentration (0.75U/L) was 6.4% and therefore functional sensitivity must be significantly less than this value.

COMPARABILITY

150 patient serum samples were analysed for LH and FSH using Olympus and AutoDELFIA methods. Correlation analyses performed showed excellent agreement between the two methods:

Olympus LH U/L = 0.95 AutoDELFIA LH + 0.016U/L ($r = 0.986$, $P < 0.0001$), Olympus FSH U/L = 1.09 AutoDELFIA FSH + 0.27U/L ($r = 0.995$, $P < 0.0001$).

Samples (50) supplied by UKNEQAS were assayed by the Olympus method and results compared to the All Laboratory Trimmed Mean (ALTM). Results were in close agreement, with correlation coefficients (r) of 0.937 ($P < 0.0001$) and 0.998 ($P < 0.0001$) for LH and FSH, respectively. Recovery of LH IRP 80/552 and FSH IRP 94/632 in UKNEQAS samples varied between 80-75% and 88-95%, respectively.

CONCLUSION

In conclusion, studies evaluating these new LH and FSH assays show excellent precision, sensitivity, and comparability with competitor assays.

Title: Evaluation of the Olympus AU3000i Immunoassay System for Serum Free Thyroxine and Thyroid Stimulating Hormone

Authors: Cundick J, Gamble R, Leslie H, Sheridan B.

Address: Endocrine Laboratory, Department of Clinical Biochemistry, Royal Victoria Hospital, Belfast, Northern Ireland.

Email: jennifer.cundick@bll.n-i.nhs.uk

INTRODUCTION

New Olympus assays for serum free thyroxine (fT4) and serum thyroid stimulating hormone (TSH) on the AU3000i analyser were evaluated in terms of imprecision, sensitivity, and comparison with results from PerkinElmer® AutoDELFIA and results from samples supplied by UKNEQAS (Birmingham, UK).

IMPRECISION/SENSITIVITY

For fT4, 10 pools (range 5.0-70pmol/L) were assayed on 10 occasions and the CVs ranged from 11.3-1.5%. The CV for the lowest value pool (5.0pmol/L) was 11.3% and therefore the functional sensitivity must be significantly less than this value. For TSH, 13 pools (range 0.02-50mU/L) were assayed on 10 occasions and the CVs ranged from 7.4-2.5%. The CV for the lowest value pool (0.02mU/L) was 7.4% and therefore the functional sensitivity must be significantly less than this value.

ACCURACY

300 patient serum samples were analysed for fT4 and TSH using Olympus and AutoDELFIA methods. Correlation analyses performed showed excellent agreement between the two methods:

Olympus fT4 pmol/L = 0.86 AutoDELFIA fT4 + 5.5pmol/L ($r = 0.859$, $P < 0.0001$), Olympus TSH mU/L = 1.03 AutoDELFIA TSH + 0.10mU/L ($r = 0.997$, $P < 0.0001$).

Samples (30) supplied by UKNEQAS were analysed and compared with the All Laboratory Trimmed Mean (ALTM). Results were in close agreement, with correlation coefficients (r) of 0.991 ($P < 0.0001$) and 0.999 ($P < 0.0001$) for fT4 and TSH, respectively. Recovery of TSH IRP 81/565 in UKNEQAS samples varied between 100-104%.

CONCLUSIONS

In conclusion, studies evaluating these new fT4 and TSH assays show excellent precision, sensitivity, and comparison with competitors' assays.

Title: Measurement of Urinary Free Cortisol by Abbott ARCHITECT and determination of reference ranges for 24 hour urinary free cortisol and for early morning urine samples cortisol:creatinine ratio.

Authors: Kilpatrick KWE, Brown C, Leslie H, Magill A, Cundick JF, Young IS, Sheridan B.

Address: Regional Endocrine Laboratory, Royal Group of Hospitals, Belfast Health and Social Care Trust.

INTRODUCTION

Urinary Free Cortisol (UFC) is a measure of the excretion of unconjugated unmetabolised cortisol. It has been shown to be the most reliable single index of adrenocortical hypersecretion and is generally accepted as being a measure of the free fraction in plasma. For these reasons measurement of UFC is widely used in the diagnosis of Cushing's syndrome. Immunoassays overestimate UFC due to multiple cross-reactants even if the urine samples are extracted, prior to analysis. HPLC methods give a true value for UFC.

AIM

To establish reference ranges for 24 hour UFC excretion and cortisol:creatinine ratio in early morning urine samples, using a new method (unextracted, chemiluminescent microparticle immunoassay) developed for use on Abbott ARCHITECT System, and to compare this with an existing routine Orion Spectria radioimmunoassay method and an in-house HPLC research method.

METHOD

One hundred and eleven 24 hour urine collections from healthy normal subjects and 415 early morning urine samples, which were previously analysed using Orion Spectria radioimmunoassay kit and in-house HPLC were analysed using this new method.

RESULTS

Each method was compared with the other two methods using Bland Altman plots.

Linear regression comparing ARCHITECT vs RIA gave $y = 0.537x + 4.77$, $r = 0.88$; for HPLC vs ARCHITECT $y = 0.5556x + 0.88$, $r = 0.87$ and for RIA vs HPLC $y = 2.3386x + 34.09$, $r = 0.87$.

The reference ranges (2.5th - 97.5th percentile) for urinary free cortisol excreted in 24 hours and cortisol:creatinine ratio in early morning urine samples, for each method, are tabulated below:

	Spectria range	ARCHITECT* range	HPLC range
Cortisol/24hr (nmol/24hr)	87.2-340.6	<20-196.6	19.3-108.7
Early morning urine Cortisol/Creatinine ratio	3.3-34.3	<20.1	0.51-12.5

*n=90 as 21 results <20 nmol/L (Functional sensitivity of assay).

If creatinine in early morning urine samples was <4mmol/L then associated results were removed for calculating reference range.

CONCLUSION

The Abbott ARCHITECT, unextracted, UFC method proved to be analytically acceptable. The reference range for urinary free cortisol employing Abbott ARCHITECT method is <20 - 196.6nmol/24hr and for cortisol:creatinine ratio in early morning urine samples <20.1 nmol cortisol/mmol creatinine. These are both significantly lower than the Orion Spectria method (87.2-340.6 nmol/24hr and 3.3-34.3 nmol cortisol/mmol creatinine). The ARCHITECT results are 57% (SD 15%) of those obtained using Orion Spectria method. The HPLC method results are only 59% (SD 21%) of those obtained using the ARCHITECT assay and the HPLC method gives results which are only 33% (SD 13%) of the Orion Spectria method. This suggests that the antibodies used in the ARCHITECT assay are more specific than those used in the Orion Spectria method and more compatible with the true values obtained by the HPLC method.

Title: Chronic kidney disease and its effect on bone turnover in an elderly outpatient population.

Authors: Healy MJ¹, Cronin H², Brewer L², Cox G¹, Walsh JB², Crowley VEF¹, Casey MC².

Address: ¹Biochemistry Department, St. James's Hospital, Dublin 8
²Mercer's Institute for Research on Ageing, St. James's Hospital, Dublin 8.

INTRODUCTION

The prevalence of chronic kidney disease (CKD) increases with age. According to NHANES III 17% of all patients over 60 years have a creatinine clearance (CrCl) <60ml/min (Stage 3 CKD). Manifestations of skeletal abnormalities begin early in CKD and the recent K/DOQI guidelines recommend that patients with Stage 3 CKD should be investigated for bone disease.

AIM

The aims of this study were to document the prevalence of CKD in an older population attending a bone clinic and to evaluate bone turnover markers, bone mineral density (BMD), and vertebral fracture risk in patients with mild CKD (CrCl > 60 ml/min) compared to those with moderate to severe CKD (CrCl < 60 ml/min).

METHOD

The charts of all new patients over 60 years referred to the St. James's Hospital Bone Clinic between March 2003 and February 2006 were reviewed. Patients with prior exposure to bisphosphonates were excluded. 175 patients (78.9±7.6 years) were included in the study. All had PTH, vitamin D, bone turnover markers (CTX, osteocalcin, P1NP) and BMD at the hip and spine evaluated. The study population was divided into 2 groups according to CrCl; group 1 <60 ml/min [n=131] (75% of total) and group 2 >60 ml/min [n=44] (25% of total).

RESULTS

BMD at both hip and spine was significantly lower in group 1 compared to those with mild CKD. PTH and vitamin D concentrations were similar in both groups. However, 75% of all 175 patients had vitamin D concentrations in the insufficient range (<75 nmol/l). Osteocalcin and P1NP were significantly elevated in group 1 versus group 2 indicating increased bone turnover in the patients with moderate to severe CKD.

CONCLUSION

These findings support the view that patients with moderate to severe CKD should be evaluated for evidence of bone loss and they should be advised concerning fracture prevention strategies.



Title: Comparison of Alternative Methods of Determining Plasma Transferrin Saturation for the Biochemical Assessment of Iron Overload

Authors: Balfe A, MacNamara B, Crowley V.

Address: Biochemistry Dept, LabMed Directorate, St. James's Hospital, Dublin 8

INTRODUCTION

Iron circulates in plasma bound to transferrin. Normally transferrin is about 30% saturated with iron. Increased transferrin saturation (TS) is an early marker of iron accumulation. Determination of TS by assay of serum iron and total iron binding capacity (TIBC) is well-established for diagnosing iron overload conditions, including hereditary haemochromatosis. Alternative approaches using assay of the unsaturated iron binding capacity (UIBC), or transferrin immunoassay, which historically lacked reliable calibrators, are now available with improved calibration. This study compares the performance of automated assays for transferrin and UIBC with the TIBC method.

METHODS

192 patient samples were assayed using Roche Diagnostics kits and the Modular P analyser. Plasma iron and UIBC were determined colorimetrically using ferrozene. TIBC was assayed using ferrozene after pre-saturation of plasma with iron. Transferrin was assayed immunoturbidometrically. TS was calculated from the iron concentration and (i) the measured TIBC concentration, or (ii) the UIBC concentration, or (iii) the transferrin concentration, using three alternative conversion factors - the theoretical factor, the kit-specified factor, and a factor determined by linear regression. The TS values were compared using the paired Student's t-test.

RESULTS

Compared to TS calculated from measured TIBC concentrations, TS calculated from UIBC concentrations showed a positive bias of +1.28%, and TIBC calculated from UIBC showed a negative bias of -1.76 $\mu\text{mol/L}$. TS calculated from transferrin concentrations using the kit factor showed a negative bias of -1.98% and calculated TIBC showed a positive bias of +2.64 $\mu\text{mol/L}$. The bias was lower using a factor determined by linear regression and much greater using the theoretical factor.

CONCLUSION

Although statistically significant ($P < 0.001$), the mean difference between the TS derived from UIBC or transferrin concentrations, and TS derived from measured TIBC has minimal clinical significance, and produced no major discrepancy in classifying patients. Based on cost the UIBC method was chosen to replace the TIBC method, with a small increase in the chance of false positives and a decrease in false negatives at the TS cut-off of 45% that indicates possible iron accumulation.

Title: Does 'Normal' Fasting Glucose Out-Rule Glucose Abnormalities.

Authors: McGing P¹, Al-Agha R², Wright E¹, Kinsley B², Kyne F¹.

Address: ¹Biochemistry Department and ²Department of Diabetes and Endocrinology
Mater Misericordiae University Hospital, Eccles Street, Dublin 7.

INTRODUCTION

Early detection of patients with Diabetes Mellitus (DM) and pre-diabetes (Impaired glucose tolerance -IGT & impaired fasting glucose -IFG) enables early intervention and improves morbidity and mortality. Fasting glucose measurement (FGlu) is often used as a convenient screen for glucose abnormalities. In an audit of GTTs in 2004 we found where the FGlu was normal (<6.1 mM) the 2hr Glu was normal (<7.8) in <2/3 of cases. In 2003, ADA has proposed lowering the fasting threshold to <5.6mmol/L.

METHODS

We looked at all GTTs performed during 2004 (n=736) and 2006 (n=886). Results were classified as normal (N), IFG, IGT or DM according to WHO criteria. Our GTT protocol involves giving 75g anhydrous glucose as 394mL.

RESULTS

For patients with FGlu<6.1 the 2hr sample indicated IGT or DM in 39% of cases for both 2004 and 2006 (mean 28% IGT and 11% DM). Application of the revised ADA criteria changed 17% of patients from normal to IGT. Almost half of these had an abnormal 2h Glu (32% IGT, 13%DM) and would now be detected as abnormal glucose homeostasis by fasting glucose alone. However, even with the revised criteria 1 in 7 patients with FGlu<5.6 during GTT had abnormal 2hr Glu (11% IGT, 3% DM).

CONCLUSION

GTT is more sensitive for the diagnosis of DM than fasting plasma and should remain the test of choice to out-rule impaired glucose homeostasis. More data looking at both microvascular and macrovascular outcomes in relation to fasting and post load glucose values are still needed to clarify the diagnostic methods.

Title: Interference with Lactate Measurement in a case of Ethylene Glycol Poisoning.

Authors: McGing P¹, Dillon-Murphy R¹, Phelan D², Colreavy F², Marsh B², Maguire S¹, Collier J¹.

Address: ¹Biochemistry Department and ²Department of Intensive Care Medicine Mater Misericordiae University Hospital, Eccles Street, Dublin 7.

CASE REPORT

A 28-year-old man (J.K.) was brought to A&E on a Sunday morning, having been found unconscious just an hour previously. Of note on admission was a profound metabolic acidosis (pH=6.78, TCO₂=5 mmol/L) with high Anion Gap (AG=33mmol/L). A toxicology screen taken at the same time proved negative (courtesy of Beaumont Hospital).

On the basis of the high AG, plus a late-reported history of possible anti-freeze ingestion, an osmolality was requested (to calculate osmolal gap) and ethylene glycol was requested on the sample sent for toxicology. Osmolal Gap was high, and ethylene glycol was subsequently confirmed (229mg/dL [37mmol/L]). Treatment was started, and despite an initially stormy progression he was discharged from hospital well, 31 days after admission.

LACTATE ANALYSIS

Serial measurements over the first few hours showed wildly fluctuating results (range 1 to 14 mmol/L). When one sample was checked for lactate on all four 'blood gas' analysers (Nova CCX) in ITU/HDU results of 3.7, 1.4, 12.1, and 7.6 mmol/L were obtained.

DISCUSSION

Glycolic acid is the main toxic metabolite of ethylene glycol and is the major cause of the characteristic severe acidosis. In following up discrepant lactate results we unearthed interference with the lactate membrane from glycolic acid. This interference had been documented in the literature (Morgan et al, Crit Care Med 1999;27,2177-9) but was not widely recognised. On foot of this case Nova modified their user manual. This case also illustrates the importance of laboratory scientific staff being involved in point of care testing.

Major fluctuations in serial lactate results should alert staff to the possibility of glycolic acid poisoning and so alert to the possibility of ethylene glycol poisoning. We would also recommend that lactate measurement not be undertaken in cases of ethylene glycol ingestion unless the method has first been shown not to be subject to interference from glycolic acid.



Title: Aetiology of acute hypoglycaemia: Re-audit of procedures for diagnosis
Authors: Lang T¹, Cardy D¹, Carson D², Leslie H¹, Loughrey CM¹, Sheridan B¹.
Address: ¹Department of Clinical Biochemistry and ²Department of Paediatrics, Belfast Health and Social Care Trust, Belfast.

INTRODUCTION

A protocol exists for the collection of samples to investigate non-diabetic hypoglycaemia, termed the "hypopack". These packs are kept in A&E departments and neonatal SCBUs throughout the region and most wards of our children's hospital. A retrospective audit of 107 hypopacks received between July 2001 and Dec 2003 highlighted a numbers of problems: samples collected when patient was receiving dextrose, incomplete clinical history, insufficient and haemolysed samples and filing of reports in patient's charts. These were addressed by redesigning the request form, updating the protocol and introducing a summative report. The new protocol was introduced in April 2006 and was supported by presentations to regional centres in Northern Ireland.

AIM

1. To review the new procedures for the distribution and analysis of hypopacks.
2. To audit the first 100 new hypopacks and determine the cause of hypoglycaemia.

METHODOLOGY

A retrospective audit of 100 Hypopacks received between April 2006 and May 2007 was performed to assess whether all samples were analysed and reported, and were taken when the patient was hypoglycaemic. Charts were reviewed to determine the cause of hypoglycaemia and to check reports were filed appropriately.

RESULTS

49% of patient were hypoglycaemic (<2.6mmol/L) compared to 35% in the original audit. 64% of patients had samples taken before dextrose compared to 54% previously. Haemolysed insulin samples remained a problem with 21% of samples being rejected. In both audits 35% of laboratory reports were missing from patients charts. Intrauterine growth retardation was the most common problem in neonates (67% of Royal Jubilee Maternity Hospital patients) and fasting due to gastroenteritis the most common in children (29% of Royal Belfast Hospital for Sick Children patients). One case of a MCAD was discovered and two endocrine related cases identified.

CONCLUSIONS

The new hypopack protocol has increased the number of appropriately performed investigations. Provision of clinical history and information concerning dextrose infusion has assisted with the interpretation of the hypopack results.

Title: Audit of Biochemical Investigations in the Management of Obstetric Cholestasis

Authors: Costa J¹, Lang TF², Hunter A¹

Address: ¹Department of Obstetrics and Gynaecology and ²Department of Clinical Biochemistry, Belfast Health and Social Care Trust, Belfast

INTRODUCTION

Obstetric cholestasis (OC) is a multifactorial condition in pregnancy presenting with intense pruritis with no rash. Liver function tests (LFTs) are often elevated and diagnosis made by exclusion of other causes of pruritis and elevated LFTs. The Royal College of Obstetricians and Gynaecologists published guidelines for the management of OC in 2006.

AIM

1. Identify patients with OC who attended RMJH in 2005
2. Evaluate current management of OC in RJMH with the RCOG
3. To develop clear diagnostic protocol to follow, in order to diagnose the disease and to develop local guidelines for the management and follow up of OC.

METHODOLOGY

1. Retrospective audit of LFTs performed in all patients attending RJMH for management of pregnancy during 2005.
2. Chart review of all patients identified with altered LFTs.
3. Fetal delivery and outcome data collected on subjects identified with OC.

RESULTS

138/1663 patients had abnormal LFTs during 2005. 23 cases of OC were identified. However 52% of patients did not have any investigations to exclude other liver pathology. Only 1 patient had bile acids measured. 52% of patients had labour induced with 26% having emergency CS. 17% of fetuses had failure to progress and 9% had abnormal CTG. 21% were admitted to neonatal unit.

CONCLUSIONS

All pregnant women presenting with pruritis should have LFTs done during 1st presentation. Bile acids should be measured locally as levels $>40 \mu\text{mol/l}$ are associated with increased fetal compromise. Other causes of liver pathology should be excluded (viral screen, autoimmune screen, liver US) before making the diagnosis of OC. Agreed local protocol should be implemented for diagnosis, management and follow up of OC based on RCOG guidelines.

Title: A case of Nephrotic Syndrome from Childhood to Adulthood

Authors: O'Keane M, Collier G, Cunningham SK.

Address: Biochemistry Department, St. Vincent's University Hospital, Dublin

INTRODUCTION

Nephrotic Syndrome (NS), which is categorized into primary (PNS) and secondary forms, is characterized by massive proteinuria, hypoalbuminaemia, oedema, and hyperlipidaemia. The subcategories of PNS are based on histologic descriptions, but clinical-pathological correlations have been made; the secondary forms are associated with complications of various systemic diseases. The criteria for the syndrome are the excretion of more than 3.5g of protein in a 24-hour period. According to the International Study of Kidney Disease in Childhood (ISKDC) the lowest amount of urinary protein consistent with the diagnosis in children is 1g/m²/d.

CLINICAL PRESENTATION

In 1994 a 35-year-old male presented with periorbital and peripheral oedema due to a relapse of the Nephrotic Syndrome and was admitted for assessment to the Nephrology Department in St Vincent's University hospital.

PREVIOUS HISTORY (1969)

Aged 11, he had been diagnosed with minimal change nephritic syndrome (MCNS).

INVESTIGATIONS

Renal ultra sound was normal. ECG and chest x-ray were normal
Urinary Protein 26.34 g/24 Hours, S.Creatinine 146 µmol/L, Urea 19.5 mmol /L
Alb 17g/L, Calcium 1.95 mmol/L, Cholesterol 19.5mmol/L
Urine culture - urine hyaline casts

A core tissue was triaged for renal biopsy: Light microscopy showed focal segmental areas of sclerosis of the glomerular tufts, while electron microscopy revealed foot process obliteration. Immunofluorescence showed IgM together with C3.

DIAGNOSIS

Nephrotic Syndrome secondary to Focal Segmental Glomerulosclerosis (FSGS).

MANAGEMENT

He responded to high-dose corticosteroids (Prednisolone) followed by maintenance dose therapy. His previous relapses had also responded to steroid therapy.

COMPLICATIONS (1998)

DEXA scan showed that the patient had developed osteopenia secondary to steroid therapy and in 2006 another complication was proximal myopathy. A further relapse in 2007 was treated with immunosuppressive therapy (Cyclosporin) combined with a slow reduction in the steroid therapy.

This case demonstrates that Nephrotic syndrome is a chronic illness characterized by relapses and remissions, which extends throughout childhood and continues into adulthood and also the adverse effect of prolonged steroid therapy.



Title: A Comparative Study between Measured Creatinine Clearance and eGFR assessed by MDRD Formula in different cohorts of Individuals

Authors: Collier G, Reece R, Cunningham SK.

Address: Biochemistry Department, St. Vincent's University Hospital, Dublin

INTRODUCTION

The gold standard methods for the measurement of true GFR are expensive, technically demanding and unsuitable for identification of chronic kidney disease in the 'at risk' population. The National Kidney Guidelines recommend the use of prediction equations to estimate GFR, in particular the 4 variable MDRD formula, which corrects for age, gender, ethnicity and is normalised to body surface area. It is known that the accuracy and performance of this equation compared to gold standards methods varies depending on kidney dysfunction.

AIM OF STUDY

The aim of this study was to assess the correlation and bias between measured creatinine clearance in a timed urine sample (the standard method in most labs) and GFR estimated by MDRD formula in subjects with different levels of renal function.

METHODS

We calculated eGFR by the MDRD formula adjusted for our creatinine method on the Roche Modular in approximately 170 patients. Creatinine Clearance (CrCl) was measured on a timed 24-hour urine sample.

RESULTS

In patients with normal renal function, ($\text{CrCl} > 90 \text{ mls/min}$) the eGFR underestimated GFR by approximately 28% compared to measured creatinine clearance. In addition the correlation between CrCl and eGFR was weak ($r = 0.35$). In patients with staged kidney disease, ($\text{eGFR} < 60 \text{ mls/min/1.73m}^2$) there was good correlation between both methods ($r = 0.59$) with eGFR having a negative bias of 5%. In patients with eGFR between 60 - 90 mls/min/1.73m² the correlation between both methods was good ($r = 0.57$). There was a proportional negative bias between eGFR and CRCL, becoming more negative at higher levels of renal function.

CONCLUSIONS

This small study showed that eGFR has a negative bias in subjects with normal renal function compared to measured creatinine clearance. The MDRD formula accurately predicts GFR in those patients with CKD but as is already known the use of different prediction equations is necessary for the optimal prediction of GFR in different patient cohorts.

Title: Glucose Tolerance Testing in Pregnancy

Authors: O’Kelly RA, Kinsley BT.

Address: Coombe Women’s Hospital, Dublin 8.

INTRODUCTION

Gestational Diabetes (GDM) is defined as glucose intolerance first recognised during pregnancy. Glucose tolerance testing is used to identify such patients. Several sets of criteria are in common use: from the National Diabetes Data Group (NDDG), the World Health Organisation (WHO) and the American Diabetes Association (ADA). The NDDG and WHO use converted O’Sullivan and Mahan data while the ADA uses the Carpenter/Coustan criteria. Positive diagnosis of GDM requires that 2 or more values meet or exceed the thresholds; however patients with only one abnormal value (Impaired glucose tolerance in pregnancy, IGT) may show increased risk of macrosomia and may benefit from intensive management. The aim of the study was to compare the rate of abnormal tests (GDM and IGT) using the different criteria.

METHODS

Pregnant women with risk factors such as family history and large for dates were tested using the 100g (as Lucozade) 3-hour glucose tolerance test (GTT) from 28 weeks of gestation. Results from GTTs over a 2-year period (2005-2006) were obtained from the laboratory information system and reviewed.

RESULTS

The number of GTTs increased by 7.5% from 2005 to 2006. Using NDDG criteria the prevalence of GDM rose from 1.0% to 1.2% over the 2 years while using lower ADA criteria, the prevalence rose from 1.7% to 2.3 %. The most common clinical details supplied on patients with a positive GTT were family history, “large for dates” and glycosuria. 206 patients (2.6%) in 2005 and 270 patients (3.3%) in 2006 had one glucose result that met or exceeded NDDG criteria (IGT), an increase of 31%. These patients went forward for further testing and management. Applying ADA thresholds to 2006 data would have seen 67 (25%) more patients with IGT undergoing further management.

CONCLUSION

As well as an increase in GTT requests, there was a larger increase in the number patients with one raised result (IGT) who required further testing. If the ADA limits were introduced, this would increase the number of glucose requests from maternity patients by another 25%. A follow-on increase in fructosamine and HbA1C requests may also occur. This would need to be balanced against patient outcomes such as macrosomia and the effect of labelling more women as gestational diabetics.



Title: Painting with Numbers - Workload Analysis across Pathology

Authors: Lanigan O.

Address: The Laboratories, Mater Misericordiae University Hospital, Dublin 7

INTRODUCTION

Laboratories must combine "broad brush pictures" with answers to detailed managerial queries. It makes sense to generate data in coherent format, one master data sheet for each section; and use that data to answer many questions.

METHODS

Data was captured from the pathology computer system (Telepath plus in-house software), from stand-alone Excel spreadsheets and from manual records. I used standard Excel Pivot Table Wizard to summarise and tabulate data, and Chart Wizard to produce coloured pictures.

RESULTS AND DISCUSSION

I worked with Biochemistry, Endocrine, Haematology, Histology, Immunology, Microbiology, Transfusion and Onward Referral (Dispatch). Each section had evolved its own approach to workload counting and analysis. After much work, all computerised sections agreed to use Telepath Sets (combined tests and profiles) as their basic count unit. Thinking hard about the questions they expect to answer, each next grouped its work counts by clinical purpose; examples Renal, Thyroid, Other Coagulation, Cytology, Allergy, Swabs, Platelet Products. One section also set up groups for costing; example Nephelometry.

Clinical User groups reflected the hospital's own Cost Centres, example CardioThoracic Surgery, and carried data on financially critical Source; examples A/E, Day Cases, GP, External site.

Three fundamental problems remain to be solved. Data for Transfusion record episodes but not quantity. Telepath analytical codes change constantly, with no laboratory computer manager or code registry. Onward referred work is logged in simple Excel files (example: Sent to UK) of uncoded free text.

CONCLUSION

Coloured charts are intuitive, they help laboratory managers to spot and follow up unexpected trends using data they recognise and understand. Broad brush pictures are especially useful when laboratories experience difficulty sharing data, and help staff see areas for potential

Title: Negative LDL Cholesterol Estimated using the Friedewald Equation.

Authors: Maguire OC¹, Mc Carthy D², Cunningham SK¹.

Address: ¹Department of Biochemistry, ²Department of Haematology, St Vincent's University Hospital, Dublin.

CASE REPORT

A 35 year old male was found to have a negative LDL cholesterol level (-0.05 mmol/L) when estimated on a fasting plasma sample using the Friedewald equation; Total and HDL cholesterol 1.0 and 0.32 mmol/L respectively, Triglycerides 1.60 mmol/L. Plasma urea, electrolytes and LFT's were normal except for a raised total bilirubin of 74 μ mol/L. Haematological results included a low haemoglobin, 7.3g/dl, low red cell count, $2.43 \times 10^{12}/L$ and low fibrinogen 0.58g/l. It transpired that the patient had undergone daily treatments of plasmapheresis for the four previous days; 4.5 litres of plasma had been exchanged with a 5% albumin solution on each occasion. He had been diagnosed with Evan's Syndrome previously (characterised by immune thrombocytopenia and haemolytic anaemia) and had been admitted with severe anaemia which had proved unresponsive to conventional treatments. Within two weeks he had responded to red cell infusions and by 10 weeks, his haemoglobin was 15 g/dl.

The rate of return of plasma analyte concentrations to steady state levels post plasmapheresis is dependent upon the number and frequency of treatments, the analyte's intra/ extra vascular distribution and de novo synthesis. The concentration of most plasma components is reduced by 50-60% after an exchange of one plasma volume. GGT (144 to 34 IU/L) and ALT (327 to 37 IU/L) levels were reduced to normal in the patient above with total bilirubin being reduced by 82 % (417 to 74 μ mol/L). The finding of a negative LDL presumably illustrates the more efficient removal of LDL and HDL lipoproteins than lipoproteins containing proportionally more triglycerides, as the latter concentration was within reference limits. Lipids, total protein, Immunoglobulin G, M and A and transferrin had recovered to steady state concentrations by 8 days post plasmapheresis whereas caeruloplasmin levels had not.

This case report illustrates the difficulties of obtaining accurate information on the steady state concentrations of plasma analytes, in particular protein bound substances, when analysis is carried out on a patient that has recently undergone plasmapheresis. The normal plasma albumin in this situation does not flag the possibility of the sample being artifactually diluted. From the data presented here, it would appear that the concentrations of some plasma proteins may take longer than 8 days to reach steady state levels post plasmapheresis.



Title: Investigation into causes of interference in the Roche E170 female testosterone assay

Authors: Joyce C, Stapleton MT, O'Mullane J.

Address: Biochemistry Department, Cork University Hospital

INTRODUCTION

There are well-documented difficulties in measuring testosterone in women using direct (non-extraction) immunoassays. Testosterone immunoassays are thought to be positively biased due to cross-reactivity with an unidentified interfering substance. This study compared female testosterone results by electrochemiluminescence (ECL) and mass spectrophotometry (LC/MS) and investigated the contribution of DHEA-S and androstenedione to interference in female testosterone measurements.

METHODS

Female testosterone samples in our laboratory are routinely analysed on the Roche E170 modular system using ECL. Samples with testosterone results ≥ 3.0 nmol/L are considered clinically significant and results are re-checked by LC/MS prior to reporting. 270 samples were analysed by both methods over a 12 month period. 65 of these samples were re-assayed for DHEA-S and androstenedione using the Immulite 2000 analyser. Results were analysed by Passing-Bablok regression analysis and Pearson correlation using Analyse-It software.

RESULTS

Regression equation for differences in testosterone, using LCMS as the reference method is $y = 0.91x + 1.93$. Pearson correlation analysis showed strong association between DHEA-S ($r = 0.57$, $p < 0.0001$) and differences in testosterone but a weak association with androstenedione ($r = 0.08$, $p = 0.545$).

CONCLUSIONS

DHEA-S or one of its metabolites significantly interferes in the Roche female testosterone assay.

Title: Clinical and Biochemical Characteristics of Moderate-Severe Hypercalcaemia in a Large Dublin Teaching Hospital

Authors: Lims S, Srinivasan S, Gannon P, Crowley VEF

Address: Biochemistry Department, St James's Hospital, Dublin 8

INTRODUCTION

Most hypercalcaemia is caused by either malignancy or primary hyperparathyroidism (1°HPT), but the relative proportion may depend on whether the patient is hospital or community based and the plasma calcium level. A range of biochemical tests including plasma PTH levels can be useful in elucidating the underlying cause of hypercalcaemia. We undertook a review of moderate-severe hypercalcaemia {Plasma corrected Ca (CorrCa) > 3.00mmol/L} in a large academic teaching hospital to determine the underlying aetiopathogenesis and the biochemical characteristics of this condition.

PATIENTS

All patients with a CorrCa > 3.00mmol/L at any stage over a defined six-month period were identified through the LIS. The patient's clinical and biochemical records were then assessed to determine diagnosis and outcome. In total twenty-two patients were identified in the study.

RESULTS

In 14/22(64%) hypercalcaemia was associated with underlying malignancy. Of these patients, 7/14 had clear evidence of bone metastases. 1°HPT was a pathogenic factor in 3/22 (14%) of subjects while 5/22 (22%) had hypercalcaemia related to other causes, primarily associated with dehydration and acute renal failure. The range of CorrCa levels was 3.05-4.51mmol/L in malignancy and 3.03-3.22mmol/L in 1°HPT. In addition, in all 3 cases of 1oHPT the plasma PO4 levels were low, but only 4/14(29%) of the malignancy group demonstrated this. Plasma PTH levels were inappropriately elevated in the 3 subjects with 1°HPT (136-325pg/ml). Plasma PTH was only analysed in 4/14 subjects with malignancy but in each case the level was low or low normal (3.1-16.6pg/ml).

CONCLUSION

Moderate or severe hypercalcaemia in a hospital environment is principally caused by malignancy and is associated with a poor prognosis. However, 1°HPT may also manifest in this manner and the presence of a low plasma PO4 is suggestive of this. Moreover, plasma PTH appears to be a very useful discriminator between these subgroups and should be analysed in all cases where the diagnosis is not apparent.

Title: Variant Maple Syrup Urine Disease (MSUD) in Three Siblings.

Authors: O'Shea A¹, O'Grady L¹, Treacy EP², Sandona N², Mayne PD¹

Address: ¹Biochemistry Department and ²National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple Street, Dublin 1

INTRODUCTION

MSUD is a rare autosomal recessive disorder caused by a deficiency of the branched-chain 2-keto acid dehydrogenase (BCKD) complex. The accumulation of the branched-chain amino acids (BCAA) and their metabolic products result in acute and chronic brain dysfunction. About 80% of patients suffer from the severe classic form with extremely low residual BCKD activities (0-2%) in fibroblasts. The remaining 20% suffer from milder variant forms with less severe clinical presentation.

CLINICAL PRESENTATION

Patient A, born of non-consanguineous Nigerian parents was detected on routine neonatal screening. Her two siblings, patients B and C, (not born in Ireland) were detected during follow-up studies.

LABORATORY FINDINGS

Neonatal screening using tandem mass spectrometry showed an elevated leucine/isoleucine in Patient A. Quantitative plasma amino acids measured on the JEOL AminoTac using ion exchange chromatography showed leucine = 395 $\mu\text{mol/L}$, (reference range 0-230), Isoleucine = 177 $\mu\text{mol/L}$ (reference range 0-105), Valine = 422 $\mu\text{mol/L}$, (reference range 0-370) and alloisoleucine = 17 $\mu\text{mol/L}$. Alloisoleucine is pathognomonic for MSUD. Follow up studies in three older siblings showed slightly elevated branched-chain amino acids and the presence of alloisoleucine in two of them (patients B and C).

Enzyme studies on skin fibroblasts showed a defect in the BCKD complex.

TREATMENT

The three siblings are on a natural protein restricted diet with high calorie regime when unwell. All are doing well and have never had an encephalopathic event.

CONCLUSION

The three patients appear to have a mild variant form of MSUD. Only one other family has this presentation in Ireland.

Title: Development of a Tandem Mass Spectrometry Method for Monitoring Plasma Glutaric Acid and 3-Hydroxyglutaric Acid in Patients with Glutaric Aciduria Type I

Authors: Finnegan N¹, Fitzsimons P¹, Monavari A², Treacy EP², Mayne PD¹.

Address: ¹Biochemistry Department and ²National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple Street, Dublin 1

INTRODUCTION

Glutaric aciduria type 1 (GA1) is an autosomal recessive inborn error of metabolism. GA1 arises from a deficiency of glutaryl-CoA dehydrogenase, an enzyme involved in the degradation pathway for lysine and tryptophan. This disorder is characterised by necrosis of the basal ganglia, occurring between 6-18 months following a trivial illness, with a resultant dystonic/dyskinetic disorder. Diagnosed patients are routinely monitored by gas chromatography mass spectrometry (GC-MS) to evaluate urinary excretion of glutaric acid (GA), an organic acid which, along with 3-hydroxyglutaric acid (3-OH-GA), is thought to be responsible for the neurotoxicity in GA1. GC-MS is a lengthy procedure and this study undertook to develop and validate a tandem mass spectrometry (MS/MS) method for evaluation of these metabolites in plasma.

METHODS

Stable isotope-labelled internal standards were added to GA1 patient plasma (n=60) and deproteinised by ultrafiltration. An acidified aliquot was injected through a C18 column and GA and 3-OH-GA levels were analysed using a Quattro Premier MS/MS. A stable-isotope dilution GC-MS method was validated as a comparison method.

RESULTS

Good linearity and sensitivity for both analytes by both methods was shown. MS/MS had excellent correlation with GA reference material (mean bias= +0.4%), compared with GC-MS (mean bias= +15%). MS/MS performed better than GC-MS in recovery experiments (GA:105%v86%; 3-OH-GA 94%v125%). Comparison plots showed a strong relationship between GA levels by both methods and a poor association between 3-OH-GA levels. Difference plots showed a negative bias for MS/MS v GC-MS. MS/MS precision was better than GC-MS for GA measurement (CV<7%) and 3-OH-GA precision was poor for both methods (CV>10%). There was no matrix effect for MS/MS. GA was stable when measured by MS/MS 24 H after sample preparation; 3-OH-GA was not stable after this time. Results for 3-OH-GA measured by MS/MS were significantly lower than for GC-MS possibly due to an interfering substance, most likely 2-OH-GA.

CONCLUSION

A simple and rapid MS/MS method was evaluated for the analysis of plasma GA and 3-OH-GA in diagnosed GA1 patients and was shown to have potential as an alternative method to monitoring urinary GA levels by GC-MS.

Title: Clinical, Biochemical and Therapeutic Experience of Pyrroline-5-Carboxylate Dehydrogenase Deficiency (Hyperprolinemia Type II) in Ireland.

Authors: Deverell D¹, Walsh R¹, Murphy A M², Hendroff U³, Treacy EP², Mayne PD¹

Address: ¹Department of Biochemistry, ²National Centre for Inherited Metabolic Disorders and ³Department of Clinical Nutrition and Dietetics, Children's University Hospital, Temple Street, Dublin 1

INTRODUCTION

There are two inherited disorders affecting proline catabolism. Proline Oxidase deficiency results in moderately elevated plasma proline levels range 600 -2000µmol/L (normal <350 µmol/L). This is known as Hyperprolinemia Type I and is asymptomatic. However in Pyrroline-5-Carboxylate(P5C) Dehydrogenase Deficiency, known as Hyperprolinemia Type II, proline levels exceed 2,000µmol/L. This condition is associated with seizures and mental retardation.

BIOCHEMICAL ANALYSIS

Ion exchange chromatography using the JEOL AminoTac amino acid analyser shows markedly elevated proline levels in plasma and iminoglycinuria (elevated proline, hydroxyproline and glycine in urine). Urinary organic acid analysis by GC/MS detects the glycine conjugate of P5C (Pyrroline-5-Carboxyglycine).

PATIENTS

There have been 12 cases of P5C dehydrogenase deficiency diagnosed to date in Ireland. Of these only 4 are attending the clinic at the National Centre for Inherited Metabolic Disorders. The ages range from 3 to 28 years. There is a wide spectrum of clinical manifestation ranging from the profoundly handicapped to the apparently asymptomatic.

THERAPY

Previous literature suggested that either P5C dehydrogenase deficiency was a benign condition or that there was no effective treatment. Our findings show this is not the case. We have attempted a treatment regime of reduced dietary protein intake. Plasma proline levels were monitored monthly.

RESULTS

Two of the four patients failed to adhere to the protein restricted diet. The remaining two patients PN and JN (siblings) reduced their natural protein intake by approx 33%. Three months into treatment their plasma proline levels have been decreased significantly. PN's proline levels reduced from 3102 µmol/L to 2394 µmol/L. JN's proline levels reduced from 2699 µmol/L to 2286 µmol/L. The younger sibling JN is reported by parents and teachers to show improved behaviour and reduction of tremor. The older sibling PN is currently asymptomatic but it is felt that reduction of proline levels may have future preventative benefits.

CONCLUSION

Initial trials of dietary protein restriction in P5C dehydrogenase deficiency show promising reduction in plasma proline levels resulting in improved clinical outcome for affected patients.

Title: Evaluation of capillary point-of-care results of electrolytes and glucose compared with laboratory analysis in a cohort of premature neonates.

Authors: Corcoran A, Bruen C, Fitzgibbon M.

Address: Department of Clinical Biochemistry, University Hospital Galway, Ireland.

BACKGROUND

Management of neonates is becoming increasingly dependent on results from point of care (POC) instruments. Sampling from a heel puncture is a useful means of collecting blood samples but requires expertise in order to obtain a quality sample. Best practice is to repeat clinically discordant results obtained at POC by laboratory analysis. It is therefore essential to provide appropriate capillary reference ranges and to evaluate how these results correlate with those obtained in the laboratory.

STUDY

Seventy seven premature neonates had simultaneous capillary samples analysed using direct ISEs on the ABL 825 FLEX and venous or capillary samples analysed using indirect ISEs on the Roche Modular. Samples were taken into pre-heparinised capillaries. Samples received in the laboratory within 3 hours of puncture were included in the study. Comparative data for sodium, potassium, chloride and glucose is presented. Fluoride oxalate was not used.

RESULTS

	Na ⁺ mmol/L	K ⁺ mmol/L	Cl ⁻ mmol/L	Glucose mmol/L
Minimum	119	2.4	94	1.7
Mean	136	4.6	107	4.8
Maximum	150	7.6	121	10.4
Slope	1.053±0.044	0.946±0.014	0.77±0.045	0.849±0.049
r ²	0.89	0.70	0.80	0.84
Regression analysis	y = 1.05x-12	y = 0.95x + 0	y = 0.77x + 25	y = 0.85x + 1.47

Regression analysis demonstrated significant intercept differences for all 4 analytes, ($p < 0.0001$).

DISCUSSION

In particular, there were a significant number of discrepant glucose results. Fluoride oxalate maintains long-term blood glucose stability but glucose levels can decline significantly in the first hours even with the use of fluoride oxalate. Therefore it is questionable as to the value of taking additional samples into fluoride oxalate in these premature infants. POC glucose using an ISE is preferable to laboratory analysis unless the sample is analysed in the laboratory immediately.

CONCLUSION

Point of care testing is expanding and provides an appropriate means of monitoring premature and neonatal populations. However, knowledge of correlation of results between methods is critical if patients are being assessed using different analytical and sampling methods.



Title: Vitamin D Status in a Healthy Female Population.

Authors: Lardner E, Wilson S, NiChadhain N, Griffin D, Grimes H, Mulkerrin E, Fitzgibbon M.

Address: Department of Clinical Biochemistry, University Hospital Galway, Ireland.

BACKGROUND

There is much evidence to suggest that hypovitaminosis D is common in Ireland and the UK. Hypovitaminosis D is an imminent risk for development of secondary hyperparathyroidism and altered bone turnover and requires timely correction of vitamin D deficiency. A significant portion of vitamin D is acquired through exposure of skin to sunlight and this is very regionally variable depending on climate.

STUDY

The aim of this study was to assess the vitamin D status in a healthy aging female population in the West of Ireland and assess the amount of secondary hyperparathyroidism in this group. One hundred and fifty caucasian women aged between 40 and 85 years with a mean age of 62 years, were randomly chosen from those attending for elective DEXA scan in Merlin Park Hospital, Galway from July to November 2006. A careful drug and supplementation history was evaluated and those treated with calcium, vitamin D, bisphosphonates and other bone altering drugs were analysed in separate sub-groups, as were those with co-existing illness including thyroid disease and diabetes mellitus.

Vitamin D was measured using the manual DiaSorin 25 Hydroxyvitamin D 125I RIA method. The assay is specific for 25OHD2 and D3 and other hydroxylated metabolites of vitamin D. PTH was measured on the Roche E170 using electrochemiluminescence immunoassay.

RESULTS

Of the 150 subjects in the study, 34 were taking calcium and/or vitamin D supplements and 16 patients were on bisphosphonate therapy.

Seventy women had no known underlying illness and were not on medication. The vitamin D and PTH results for this cohort were as follows;

	Vitamin D nmol/L	PTH pg/ml
Minimum	11	14.7
Mean	58	40.8
Maximum	110	140.9

43% of subjects were vitamin D insufficient (<50nmol/L) and only 4% were sufficient for the time of year if the recommended >100nmol/L threshold was used as the target. 16.5% of this healthy subject cohort had biochemical evidence of secondary hyperparathyroidism without biochemical abnormality in calcium and alkaline phosphatase results.



DISCUSSION

Hypovitaminosis D was found to be prevalent in this cohort of subjects and this study would suggest that it is clinically under diagnosed in the population at large. The age profile of the cohort is of particular interest as most studies of healthy subjects are performed in younger age groups. In the light of the long term impact of vitamin D deficiency on bone metabolism, all the vitamin D deficient patients particularly those with increased PTH and low BMD were recalled and commenced on calcium/vitamin D treatment as appropriate.

CONCLUSION

This study clearly suggests that more testing of vitamin D status is warranted and the development of automatable specific methods using tandem mass spectrometry will make biochemical analysis more feasible in the future.

Title: Diagnostic Output of Skin Biopsies in Inherited Metabolic Disorders.

Authors: Pitan C¹, Crushell E¹, Mayne PD², O'Neill C², Devaney D², Monavari A¹, Treacy EP¹, Olpin S³, Murphy AM¹

Address: ¹The National Centre for Inherited Metabolic Disorders (NCIMDs)
²Department of Pathology, Children's University Hospital, Temple Street
Dublin, Ireland. ³Department of Clinical Chemistry, Sheffield Children's
Hospital, Sheffield, United Kingdom

BACKGROUND AND AIMS

The performance of a skin biopsy with culture of skin fibroblasts and enzymology studies is an important step in the diagnosis of many inherited metabolic disorders. In this retrospective analysis, the skin biopsies done over a 24 month period at the NCIMDs were evaluated to determine the diagnostic output from and main indications for this invasive procedure.

METHODS

All patients who had skin biopsies performed between January 1st 2005 and December 31st 2006 at the request of a Metabolic Paediatrician were identified from the database at the department of pathology. Case records were reviewed. Age at time of investigation, clinical features, adverse incidents (infection, bleeding, specimen loss, cell failure) and biopsy results were recorded.

RESULTS

130 patients (83 male, 48 female) underwent skin biopsies during the study period. Age ranged from 2 weeks to 56 years. There were no adverse incidents. Clinical indications in order of frequency were, developmental delay 41(31.5%), hypoglycaemia 20(15.4%), positive family history of an inherited metabolic disorder 11(8.5%), seizures 8 (6.2%), cardiomyopathy 7 (5.4%), ALTE 6 (4.6%), hypotonia 5 (2.3%), liver disease 3 (2.3%), Autism 2 (1.5%) and others 27 (20.8%). A formal report was available on all patients. In 29 of the 130 biopsies the results were diagnostically relevant, 12 patients were assigned a definite diagnosis (6 fatty acid oxidation defects, 5 respiratory chain defects, 1 non-ketotic hyperglycinemia), 6 a probable/possible diagnosis and patient's 11 enzymology studies outruled a particular familial diagnosis, 3 of which were glutaric aciduria type 1. In 101 cases the diagnosis was established by other means or remained unclear.

CONCLUSION

The diagnostic output was 22.3%. The main factor for a conclusive result is the indication for the biopsy. This investigation remains a cornerstone in the pathway to a diagnosis of an inherited metabolic disorder.



Notes



Notes

