



**Welcome
to
ACBI 2008**
17 - 18 October 2008

**The Proceedings of the 31st Conference
of the
Association of Clinical Biochemists in Ireland**

**Radisson Hotel
Golden Lane, Dublin 8, Ireland**

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From the President of ACBI

Céad Míle Fáilte Róimh and welcome to ACBI 2008.

We have a most interesting and packed scientific programme spread over four half-day sessions. With the current public emphasis on regulation and quality in the healthcare field, it is indeed fitting that Dr. Tracey Cooper from HIQA, the Health Information and Quality Authority, will deliver the keynote address at the opening session. A session entitled "The impact of a changing ethnic population on clinical biochemistry", is a most timely focus for us, as Ireland shifts from a relatively homogenous ethnic character to a more diverse and multi-ethnic one. This is followed by a session on heart disease, with the imaginative title "from failure to rescue". On Saturday, the focus is on biochemical issues for the elderly, and finishes by going to the Front Line, placing ourselves biochemically in the Emergency Department.

On Saturday afternoon, in conjunction with Abbott Diagnostics, we will have the launch of "Labs Are Vital Ireland" a joint venture between the ACBI, the AMLS, the Faculty of Pathology and Abbott Diagnostics. The aim of this initiative is to raise the awareness and understanding of the role and contribution of the laboratory to healthcare.

After last year's successful launch, once again we will award the Geraldine Roberts Medal for the best scientific poster at the meeting.

As we all know, a conference can only come about through the efforts of many people. I wish to recognise our corporate colleagues in the diagnostics industry for their very generous support. Also, I want to sincerely thank our invited speakers, who give of their time to prepare and to present at our meeting. Thanks too to those who have presented their work at the poster sessions, an important element of the meeting. One of the great strengths of the ACBI over the years has been its active and committed membership. I commend and congratulate Dr Marguerite MacMahon and the Mater Hospital team for the excellent work they have done in organising the conference. Finally thank you to the participating delegates, I am certain that we will all go away energised after a memorable two days.

Dr Alan Balfé

President, ACBI



Continuing education

The Royal Colleges ACBI 2008 has been approved for CPD by the Royal College of Pathologists (RCPATH) and for CME by the Royal College of Physicians of Ireland (RCPI).

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

CPD: Maximum 11 credits for the two day meeting

CME Friday 17 October = 6 credits

Saturday 18 October = 6 credits

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

Academy of Medical Laboratory Sciences ACBI 2008 has been approved by the Academy of Medical Laboratory Sciences (AMLS) for the award of CPEP points. Ten CPEP points will be awarded for each day attended or 20 CPEP points for the full two day conference.

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

Evaluation of ACBI 2008 All conference participants are requested to complete the conference evaluation form provided and return it to the Conference Registration Desk. ACBI evaluates the quality and educational benefits of its meetings in order to maintain a tradition of high educational standard. This process also assists in the planning of future meetings.

ACBI 2008 conference team



Committee from left to right Kieran Halton, Rachel Cullen, Peadar McGing, Marguerite MacMahon, Mark Kilbane. Frank Kyne (not pictured).

Registration coordinator Georgia Gallagher

Concept & design John Wiles



Welcome to ACBI 2008

It gives me great pleasure on behalf of the organising committee to welcome you to ACBI 2008 the 31st annual conference of the Association of Clinical Biochemists in Ireland. A warm welcome to our invited speakers, guests, delegates, ACBI and ACB colleagues, and all attending the conference. A particular word of welcome to our corporate sponsors, their generous support is vital to ensuring the continued success of the ACBI's annual scientific and social meeting.

The ACBI members in the Mater Hospital have been entrusted with the responsibility of organising the conference after an absence of 13 years. The venue, new to ACBI, is the Radisson Royal Hotel in the heart of medieval Dublin and we hope that you may find time to visit some of the many historic sites close by over the weekend.

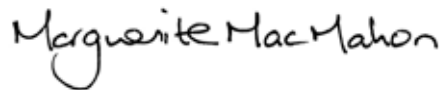
The scientific programme includes lectures on the role of biochemistry in a number of topical areas, ranging from the accident and emergency department to the challenge of adapting service needs with an increasingly elderly and ethnically diverse population. A subject close to our hearts in the Mater is the role of biochemistry in coronary care and heart/lung transplantation. We hope the scientific content, case and poster presentations stimulate your interest.

As part of our social programme we have organised two contrasting evening events. On Friday evening we will be at the famous Chester Beatty Library where a private viewing of the collection has been arranged. The gala dinner will be held in the Radisson Hotel on Saturday evening.

This year is the first without Maire Oakley who has retired from the position of ACBI Conference Secretary after some 20 years. Maire was a familiar face to all our members over time and we wish her well.

Our thanks to the outgoing committee in the Children's University Hospital, Temple Street, Dublin for their advice and guidance in the handover period.

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

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

Dr Marguerite MacMahon (Chairperson)



Programme - 17 October 2008

8.45 Registration

Opening Ceremony

9.45 ACBI President's address - Dr Alan Balfe

10.00 Keynote address - Dr Tracey Cooper, Chief Executive, The Health Information and Quality Authority

Session 1 The impact of a changing ethnic population on clinical biochemistry

Chairperson - Ms Anne O'Shea, Children's University Hospital, Temple Street, Dublin

In recent years the population served by Irish hospital laboratories has changed from being essentially homogenous to where over 10% of the population is of non-Irish extract. This session will review the impact of this change on health care, with a particular emphasis on how it affects Clinical Biochemistry.



10.30 A public health perspective on the changing ethnic population in Ireland Dr Margaret Fitzgerald, Department of Public Health, HSE, Dr Steevens Hospital, Dublin

11.00 Tea & coffee and poster presentation viewing

11.30 Socioeconomic differences in markers of cardiovascular risk in the Greater Glasgow population Dr Kevin Deans, Specialist Registrar, Glasgow Centre for Population Health, Greater Glasgow NHS Board, Scotland

12.10 Clinical laboratory services for a multiethnic population Ms Janet Smith, Department of Chemical Pathology, Selly Oak Hospital, University Hospital Birmingham NHS Trust, England



12.50 Lunch



Programme - 17 October 2008

Session 2 Heart disease, from failure to rescue

Chairperson - Ms Helen Moore, Beaumont Hospital, Dublin

Heart failure is a major cause of morbidity in Ireland. This session will address the initial diagnosis and treatment of patients with this condition with a critical overview of the role of BNP. Discussion of patient management includes views from both the heart-lung transplant team and the drug-monitoring laboratory.

**14.00 Heart failure - a medical perspective**

Dr Niall Mahon, Consultant Cardiologist, Mater Misericordiae University Hospital, Dublin

14.40 BNP and the heart

Dr Michael Penney, Department of Clinical Biochemistry, Royal Gwent Hospital, Newport, Gwent, Wales

15.20 Tea & coffee and poster presentation viewing

Authors of posters 1 - 9 in attendance

**15.50 Advanced lung disease and lung transplantation**

Prof Jim Egan, Consultant Respiratory Physician, Mater Misericordiae University Hospital, Dublin

16.30 Measuring immunosuppressive drugs - is there any point?

Prof David W Holt, Professor of Bioanalytics, Analytical Unit, St George's - University of London, England

17.30 ACBI AGM (members only)**19.00 An evening at the Chester Beatty Library, Dublin Castle**

Starting with a private viewing of the library followed by dinner.



Programme - 18 October 2008

Session 3 Biochemistry for the elderly

Chairperson - Dr Pooler Archbold, Belfast City Hospital, Northern Ireland

The percentage of older people in this country is rising (11% in 2002 and projected to be 14% by 2011). As people age they may require considerable medical care and this can necessitate much laboratory testing. Equally, many older people remain very healthy, though with some age-related changes in their condition. In this session the role of biochemistry in the overall evaluation of health and disease in the elderly will be addressed.



9.30 **Caring for the older person in Ireland - an overview**

Dr Dermot Power, Consultant Geriatrician, St Mary's Hospital Phoenix Park and Mater Misericordiae University Hospital, Dublin

10.15 **Aspects of biochemistry tests in the elderly**

Ms Margaret McDonnell, Clinical Scientist, Belfast City Hospital, Northern Ireland

11.00 **Tea & coffee and poster presentation viewing**

Authors of posters 10 - 20 in attendance

11.30 **Management of the older person - case histories**

Dr Bláithín MacMahon, Specialist Registrar in Geriatric Medicine, St Mary's Hospital Phoenix Park, Dublin

12.15 **One foot in the....Laboratory**

Dr John Doran, Consultant Chemical Pathologist, Morriston Hospital, Swansea, Wales

13.00 **Lunch**





Programme - 18 October 2008

14.00 Exploring and explaining the value of the laboratory

Dr Graham Beastall, Department of Clinical Biochemistry, North Glasgow University Hospitals, Glasgow UK
ACBI launch of 'Labs Are Vital Ireland'

Session 4 On the front line - Biochemistry for the emergency department

Chairperson - Ms Geraldine Collier, Department of Biochemistry, Beaumont Hospital, Dublin

This session will critically examine the role of biochemistry tests in the emergency department. There will be views from both a medical and laboratory perspective, including what future developments in this area may impact on the biochemistry laboratory.



14.30 Clinical biochemistry - an emergency physicians viewpoint

Dr Eamonn Brazil, Consultant Emergency Physician, Mater Misericordiae University Hospital, Dublin

15.15 Clinical biochemistry tests in A & E - what tests and knowledge is required?

Dr Danielle Freedman, Medical Director, Department of Chemical Pathology, Luton & Dunstable Hospital NHS Trust, Luton, England

16.00 Presentation - Geraldine Roberts medal

Dr Alan Balfe, President of the ACBI

16.15 Close of conference

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

19.00 Reception and conference dinner

Radisson Royal Hotel, Golden Lane, Dublin



Keynote address



Dr Tracey Cooper
Chief Executive
The Health Information
&
Quality Authority

The Health Information and Quality Authority is led by Dr. Cooper who was appointed CEO in August 2006.

During her career Dr. Cooper has worked in and advised on a variety of different health systems, served on a number of national task forces, worked closely with health improvement bodies in the UK and with the health and social care system in Northern Ireland.

She graduated from Southampton University Medical School in 1990, and subsequently held a number of posts in General Surgery and Accident & Emergency in England and Scotland. She was Locum Consultant in A&E in Chesterfield & North Derbyshire Royal Hospital before leaving clinical practice, becoming more involved in national health reform and taking up a series of senior management posts in the NHS, including Director of Clinical Services for East Midlands Ambulance Service NHS Trust. She joined the NHS Clinical Governance Support Team in 2001 and became Deputy Head and Director of Operations in January 2004.

The Health Information & Quality Authority

The Health Information and Quality Authority (HIQA) was established on a statutory basis in May 2007 following the signing into law of the Health Act 2007 as part of the government's health reform programme and is committed to operating to the highest standards of efficient and effective corporate governance. It is an independent authority, with broad ranging functions and powers reporting to the Minister for Health.

HIQA have been set up to drive quality, safety, accountability and the best use of resources in our health and social care services, whether delivered by public, voluntary or private bodies.

HIQA has been charged with setting the standards for delivering health and social care services and it continuously inspects to ensure that these standards are being met. The findings of its inspections are published so that the public can make informed choices when seeking care and thereby deliver value for money by monitoring that the resources in our health and social services are used in a way which delivers the best outcome for the patient or service user.

Session

1

Impact of changing ethnic populations on clinical biochemistry

In recent years the population served by our hospital laboratories has changed from being essentially homogeneous to where some 10% of the population are non Irish National. This session will review the impact of this change on health care, with a particular emphasis on how it affects clinical biochemistry.

Chair

Ms Anne O'Shea

Anne O'Shea is Principal Biochemist at the Children's University Hospital, Temple Street. She is a graduate of Trinity College Dublin, where she obtained her MSc. Having worked in general Biochemistry for many years, Anne then moved into the Metabolic Laboratory in 1994. This is the national centre for the investigation of inherited metabolic disorders in children, where she specialises in amino acid analysis. Memberships include: Society for the study of Inborn Errors of Metabolism, British Inherited Metabolic Disease Group.

Speakers

Dr Margaret Fitzgerald

Margaret Fitzgerald is a consultant in Public Health Medicine in Dublin. After qualifying in Galway she worked in child health and trained in general practice in the UK before spending several years in Africa. She subsequently trained in public health medicine in Ireland and currently specialises in infectious disease surveillance and control. She has worked in the Food Safety Authority and in general public health. In 2005-6 she spent 18 months working in Malawi and has published on HIV related topics. She retains her interest in international health and development.

Dr Kevin Deans

Kevin Deans studied medicine at the University of Glasgow, including an intercalated BSc (Hons) in Medical Biochemistry. After completing MRCP(UK) he was appointed as a Specialist Registrar in Chemical Pathology and Metabolic Medicine in the West of Scotland. His main research activity is studying the associations between social deprivation and cardiovascular risk, focussing on biochemical markers of cardiovascular risk and on ultrasound assessment of carotid atherosclerosis.

Ms Janet Smith

Janet Smith is currently the Consultant Clinical Scientist and Clinical Service Lead for Clinical Biochemistry at the University Hospital Birmingham NHS Foundation Trust. She is also an Honorary Senior Clinical Lecturer at the Division of Medical Sciences, University of Birmingham. She is currently Chair of IFCC Education and Management Division and was previously Chair of the Association for Clinical Biochemistry (ACB), Chair of ACB Education Committee and Chair of ACB Regulating Committee (now FCS).

A public health perspective on the changing ethnic population in Ireland

Dr Margaret Fitzgerald
Department of
Public Health
HSE
Dr Steevens Hospital
Dublin

Currently Ireland has the fastest growing population in the European Union, from almost 3.9 million in 2002 to 4.2 million in 2006 (8% increase). Migration is the dominant factor. By 2030 almost one in 20 of the population will be foreign born compared to one in 10 at present. Ethnic minorities include asylum seekers, refugees, migrant workers, Irish Travellers, Roma, and foreign students. While 10 years ago the majority were asylum seekers, most now come in search of work.

For many of those from ethnic minorities health is not the main priority. However issues such as language barriers, access to healthcare, and discrimination and stigma, especially for black people, are important. Health needs of this diverse group are still not quantified but include specific diseases that are more prevalent in certain ethnic populations.

The HSE recently launched a National Intercultural Health Strategy with priority given to areas such as information, language and communication. The rise in the indigenous elderly population means the health service must be in a position to respond appropriately for both primary care and chronic diseases as well as with an ethnically more diverse population.

Specific disease that could affect people from ethnic minorities includes haematological diseases and infectious diseases. With people from West Africa there is an increase in congenital haemoglobinopathies, sickle cell, and thalassaemia, among others. Infectious diseases of concern include malaria, with recent increases in cases reported to the HPSC from patients returning home on holidays, also Hepatitis B cases from highly endemic countries. Hepatitis C is still mainly a disease of intravenous drug users but there are more cases in people migrating from Eastern Europe and North Africa. Newly diagnosed HIV cases also reflect the trend towards heterosexuals whose origins are from Sub Saharan Africa.

Patients from ethnic minorities also have mental health issues relating to culture, war, torture and forced labour. Certain chronic diseases such as hypertension and diabetes have high prevalences in some ethnic populations.

Hospitals and other health service managers/providers will need to take population profiles into account when planning and delivering services and when recruiting, supporting and retaining staff. In planning for the future, services need to be provided equally to all and respond appropriately to the specific health need of new and well-established minority communities.



Socioeconomic differences in markers of cardiovascular risk in the Greater Glasgow population

Dr Kevin A Deans
Glasgow Centre
for Population Health
Greater Glasgow
NHS Board
Scotland

Increased cardiovascular risk is known to be associated with higher deprivation scores. The extent to which deprivation-associated vascular changes are demonstrable by carotid ultrasound (carotid intima-media thickness [cIMT] or plaque), or explainable by putative risk factors, has been only sparsely studied.

Based on deprivation category, 666 age-matched male and female participants from the Greater Glasgow Health Board area were selected. Participants had anthropometric measurements, blood pressure, carotid ultrasound assessment of cIMT and plaque score and measurement of lipids, glucose, insulin and 'novel' biomarkers reflecting adiposity, inflammation and haemostasis.

Age and sex adjusted cIMT was significantly higher in the most deprived group ($p=0.015$), but on subgroup analysis this difference was only apparent in the highest age tertile in males (>56.3 years). Plaque score showed a much more highly significant deprivation difference ($p<0.0001$ for the group as a whole). Of the "classical" cardiovascular risk factors, neither LDL/HDL ratio nor blood pressure differed between most and least deprived groups.

Fasting glucose, waist/hip ratio and body mass index were all higher in the most deprived group. A significantly higher percentage of the most deprived group (74.4%) were smokers compared to the least deprived group (35.4%). In the most deprived group, 49% of participants were physically inactive, compared with 24% in the least deprived group.

Of "novel" risk factors, markers of insulin resistance (fasting insulin, Homeostasis Model of Assessment [HOMA-IR] and leptin); markers of inflammation/endothelial dysfunction (CRP, IL-6 and ICAM-1) and markers of haemostasis (vWF, fibrinogen and D-dimer) were all significantly higher in the most deprived group. However, when measured risk factors were incorporated into multivariate models with plaque presence as the dependent variable, neither adjustment for classical cardiovascular risk factors nor measured "novel" risk factors, either alone or in combination, abolished the deprivation-based difference in plaque score; adjusted odds ratio of 1.73 (1.07-2.82) for plaque presence in most deprived versus least.

Deprivation was associated with increased plaque score and cIMT. Differences were not explained by classical risk factors, which has implications for interventions designed to reduce socio-economic variation in health.

Clinical Laboratory Services for a multiethnic population

Ms Janet Smith
Department of
Chemical Pathology
Selly Oak Hospital
University Hospital
Birmingham

The changing population profile of Northern European countries has led to medical conditions encountered relatively rarely up to the late 20th century becoming commonplace, because they have a high prevalence in immigrant ethnic groups. Among these are inherited abnormalities, such as the haemoglobinopathies. Other conditions are acquired by individuals from ethnic groups as a result of moving to our Western society and to countries with very different climates to those they have left.

Some of these conditions, such as vitamin D deficiency, had been largely eradicated in the native population, but have now re-emerged as public health problems. Others, such as Type 2 diabetes, are worldwide health problems but some ethnic populations in UK and Ireland have an increased predisposition to the disease, and higher mortality and morbidity from it, challenging diabetes support services.

Health services should be tailored to fulfil the needs of the population and be constantly reviewed in the light of demographic changes. Clinical Laboratory Services are no exception. We need to consider our test repertoires, procedures and protocols to determine whether they are 'fit for purpose' for individuals across our multiethnic society. The increased prevalence of some inherited diseases may necessitate the introduction of new neonatal or antenatal screening programmes.

Published guidance on laboratory diagnosis and monitoring of disease may not be universally transferable across different ethnic groups, for example HbA1c in diabetes monitoring and MDRD eGFR calculations in the diagnosis of chronic kidney disease. Alternative strategies may be required.

As well as specifics relating to the analytical and clinical aspects of the service, the implications of cultural and language differences of ethnic groupings has to be considered in administration and management of the service as a whole. It may be necessary to provide translation services for documentation as well as verbal communication and care is needed in ensuring positive patient identification, as parameters we traditionally rely on for such purposes are not the norm in some other cultures.

A changing multiethnic society in the UK and Ireland is with us to stay and our health services are adapting to encompass the requirements of ethnic groupings. Clinical laboratory services must be flexible in developing and diversifying to support the required changes.



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Session

2

Heart Disease, from failure to rescue

Heart failure is a major cause of morbidity in Ireland. This session will address the initial diagnosis and treatment of patients with this condition with a critical overview of the role of BNP. Discussion of patient management includes views from both the heart-lung transplant team and the drug-monitoring laboratory.

Chair

Ms Helen Moore

Helen Moore graduated from UCD and MSc from TCD and started her career in Jervis Street Hospital, then transferred to Beaumont Hospital, Dublin. She is a member of ACBI, has been on Council and was Treasurer for 3 years. Now treasurer & secretary of the voluntary General Register of Clinical Biochemists. Interested in all aspects of Clinical Biochemistry, currently working in Tumour Markers, Haematinics with extensive experience in the area of protein electrophoresis.

Speakers

Dr Niall Mahon

Niall Mahon graduated from University College Galway in 1991, and currently is Consultant Cardiologist at the Mater Misericordiae University Hospital. His clinical and research interests include heart failure, heritable cardiovascular diseases, and the prevention of sudden cardiac death.

Dr Michael Penney

Mike Penney is Consultant Chemical Pathologist at the Royal Gwent Hospital, Newport, South Wales. He trained in biochemistry and medicine at the Universities of Birmingham and London. Post-graduate training in pathology and clinical biochemistry was in Bristol and Leeds. He has a long-standing interest in salt and water metabolism and his laboratory provides an international assay service for the measurement of arginine vasopressin and atrial natriuretic peptide.

Prof Jim Egan

Jim Egan qualified in University College Galway and he trained in Pulmonary Medicine in the North West Lung Centre, Manchester, United Kingdom. He was appointed as Lead Physician to The Irish National Lung Transplant Programme in 2000. His research interests include:- The Management of Advanced Lung Disease, particularly pulmonary fibrosis and lung transplantation. Dr Egan is currently co-chair of The American Thoracic Society / European Respiratory Society – Guideline Committee for the Management of Idiopathic Pulmonary Fibrosis. He is chairman of The Irish Transplant Society and a former chair of The European Respiratory Society Transplantation Committee.

Prof David W Holt

David Holt is the Director of the Analytical Unit and Professor of Bioanalytics at St George's, University of London, UK. He has more than 37 years' experience in the measurement of drugs as a guide to therapy and in the diagnosis of drug-induced toxicity. He has been responsible for the development of assays used to monitor the toxico-kinetics of a wide variety of therapeutic agents. Professor Holt is widely known as the organiser of International Proficiency Testing Schemes for immunosuppressive drugs. His current research interests include the development of mass-spectrometric assays for the measurement of endogenous markers of organ damage and dysfunction, pharmacogenetics, the development of methods to assess phenotypic markers of drug metabolism and the detection of drugs used in drug-facilitated crime.

Heart failure - a medical perspective

Dr Niall Mahon
Consultant Cardiologist
Mater Misericordiae
University Hospital
Dublin

Heart failure is a multisystem syndrome caused by the inability of the heart to support the circulation commensurate with the needs of the body. With increasing longevity and improved survival from other cardiac diseases, a heart failure 'epidemic' is predicted.

Cardiac failure has long been conceptualised within paradigms built around available treatments. In bygone days when the only available treatments for 'dropsy' were blood-letting, digoxin and, later, diuretics, it was largely considered a problem of volume overload.

The advent of safe and effective diuretics in the 1950s revolutionised the management of heart failure but it quickly became clear that, while relieving symptoms, diuretics did not prevent the inexorable progression to refractory end-stage failure and death. Enter the era of neuro-hormonal antagonism, where it is now understood that heart failure is a complex multisystem disease whereby maladaptive neuro-endocrine activation (in particular the renin-angiotensin-aldosterone system and the sympathetic nervous system) creates a self-perpetuating cycle of adverse remodelling.

Antagonism of these systems with ace-inhibitors and beta-adrenergic receptor antagonists has revolutionised the treatment of heart failure. More recently again, there has been focus on electrical aspects of the disease, as further improvements in prognosis have been brought about by resynchronisation therapy and devices for the prevention of sudden cardiac death.

Finally, should emerging technology allow the development of affordable and reliable mechanical or biological pump-replacement therapy, heart failure may come to be conceptualised as a simple and easily dealt with mechanical problem.



BNP and the heart

Dr Michael Penney
Department of
Clinical Biochemistry
Royal Gwent Hospital
Newport
Gwent
Wales

Natriuretic hormones were prophesised soon after the discovery of mineralocorticoids, but it was not until 1981 that a cardiac origin was demonstrated. The first peptide described was atrial natriuretic peptide (ANP), quickly followed by brain natriuretic peptide. Brain natriuretic peptide (BNP) was originally isolated from porcine brain but subsequently shown to be produced mostly in the ventricles of the heart. The regulation of BNP is at the level of gene expression, and the pro-hormone is synthesised within the ventricular myocytes in response to stretch and is released into the circulation cleaved to the physiologically active BNP and the N-terminal pro BNP (NT-proBNP): collectively these are termed B-type natriuretic peptides. BNP is an antagonist to the renin-angiotensin-aldosterone system and to the sympathetic nervous system. BNP promotes renal sodium excretion and vasodilatation; levels in plasma are influenced physiologically by dietary sodium intake, age, gender and body mass, and pathophysiologically by systolic and diastolic heart failure, by fluid overload and by deteriorating renal function.

It is estimated that just under 1 million individual in the UK have diagnosed heart failure with almost an equal number within a prodromal stage. The National Institute for Clinical Excellence (NICE) published guidelines in 2003 aimed to define best practice for the diagnosis and management of heart failure, predicting a clinical utility for B-type natriuretic peptides as a rule-out test prior to definitive echocardiography. Since then B-type natriuretic peptides have been promoted also as an objective means to guide clinical treatment of heart failure, and also as a prognostic indicator in acute coronary syndromes.

Manufacturers of clinical chemistry equipment and reagents have subsequently introduced the measurement of B-type natriuretic peptides into their automated test repertoires. However, since the NICE publication the routine adoption of B-type natriuretic peptides as a screening test for heart failure has been sporadic within the UK due to a combination of factors including high reagent costs, perverse disincentives for both primary and secondary care, and not least to concerns by laboratories that unfettered access to a B-type natriuretic peptide assay service would not be appropriately resourced.

There is a growing evidence base to support the utilization of B-type natriuretic peptide measurement in screening high risk patients for both systolic and diastolic heart failure. Laboratories will provide a pivotal future role in ensuring that cost-effective and diagnostically efficient programmes can be introduced and maintained.

Advanced lung disease and lung transplantation

Prof Jim Egan
Consultant Respiratory
Physician
Mater Misericordiae
University Hospital
Dublin

This presentation will review the Management of Advancement Restrictive Lung Disease, which is manifest by idiopathic pulmonary fibrosis, and new therapies that are emerging for the treatment of this condition.

Idiopathic pulmonary fibrosis (IPF) is a common and progressive form of chronic fibrotic diffuse disease that poses many challenges. IPF affects approximately ten per one hundred thousand of the general population.

Lung transplantation offers a lifesaving solution for IPF and the experiences within the National Heart Lung Transplant Unit in the Mater Misericordiae University Hospital will be reviewed. Currently the mortality rate amongst patients awaiting lung transplantation is highest in the pulmonary fibrosis group. Emerging studies are highlighting the importance of alternative forms of therapy. Of particular interest are new developments in the area of interventional bronchoscopy. This technique allows volume reduction in patients with advanced emphysema with the potential of bridging to lung transplantation.



Measuring immunosuppressive drugs - is there any point?

Prof David W Holt
Professor of
Bioanalytics
Analytics Unit
St George's -
University of London
England

Measurement of immunosuppressive drugs has become an integral part of transplantation medicine. Measurement of these drugs has contributed to our understanding of their clinical pharmacokinetics, enabling rational monitoring strategies to be developed. Both the diagnostics and laboratory communities have made substantial efforts to improve the methodology to measure immunosuppressive drugs, and our clinical colleagues use the measurements routinely to optimise therapy. However, it has to be acknowledged that, for ciclosporin and tacrolimus in particular, therapeutic drug monitoring (TDM) is founded on empirically derived data, without the benefit of randomised controlled trials.

Two recent studies, in which kidney transplant patients were randomly assigned to receive mycophenolic acid either with or without TDM-driven dosing, have given conflicting results. Neither of the studies was perfect, and some of the problems of study design in this clinical area will be discussed. Other large scale studies, which suggest general trends with respect to efficacy or toxicity based on drug concentration data, are often difficult to interpret in terms of the individual patient. Fortunately, there are a number of developments in the field of analytical methodology that might impact on the value of TDM in transplantation, and these will be addressed.

It will be concluded that, after a history spanning more than 25 years, TDM of immunosuppressive drugs is still an evolving field. The added value must come from a careful assessment of the data and improvements in bioanalytics, rather than a crude application of so called therapeutic concentration ranges.

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- Change management
- Redefined lean processes
- Laboratory rebuild / reconfiguration
- Total supply chain management

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Managed Service Solutions

Biochemistry for the elderly

The percentage of older people in this country is rising (11% in 2002 and projected to be 14% by 2011). As people age they may require considerable medical care and this can necessitate much laboratory testing. Equally, many older people remain very healthy, though with some age-related changes in their condition. In this session the role of biochemistry in the overall evaluation of health and disease in the elderly will be addressed.

Chair

Dr Pooler Archbold

A BSc and PhD in Biochemistry (Belfast) followed by a postdoctoral fellowship in Royal Postgraduate Medical School induced me to change course and study medicine (Belfast). The circle was completed by returning to Biochemistry and enjoying 2 years in Guildford with Professor Vincent Marks. Returned to Belfast and since 1989 he has been Consultant Chemical Pathologist in Belfast City Hospital with clinical interests in diabetes, lipidology, osteoporosis and thyroid disease.

Speakers

Dr Dermot Power

Dermot Power graduated from UCD in 1991 following which he completed postgraduate specialist training in the John Radcliff Hospital, Oxford. He was awarded an MD from UCD in 2001. Dr Power has a special interest in the management of geriatric services.

Ms Margaret McDonnell

Margaret McDonnell began with a Biochemistry degree in Queen's University Belfast, followed by MSc in analytical chemistry before employment in Biochemistry Department Royal Victoria Hospital. Training included the MSc in Trinity before the MRCPPath. She has worked in Belfast City Hospital for most of her 20 year career, with special interests in tumour markers and point of care testing. Margaret is now acting professional lead for Biochemistry in the new Belfast Trust.

Dr Bláithín MacMahon

Bláithín MacMahon graduated with an honours degree in Bachelor of Science at UCD's Department of Pharmacology, School of Science. She obtained her Ph.D in Molecular and Cell biology at the Department of Medicine and Therapeutics, School of Medicine, UCD (2002). She completed a post-doctoral Fellowship at the Conway Institute, UCD where she published in several international journals in the area of eicosanoid receptor cloning and signal transduction in human glomerular cells. She obtained her honours degree in medicine at UCD in 2006, and is currently enrolled in a senior house officer training programme at the Mater Misericordiae University Hospital and St. Mary's Hospital.

Dr John Doran

John Doran started his career as a dentist, with an interest in oral surgery. Did voluntary service in Malaysia returning to the UK to study medicine in Cardiff. Intercalated biochemistry degree signalled a change in direction, and having graduated in Medicine and achieved MRCP, trained in chemical pathology (in various other names) in Cambridge and Dundee. 17 years as single handed consultant in Peterborough, and moved to Swansea in 2006. Lots of toys, bikes, canoe, kayaks, surfboard, snowboards!

Caring for the older person in Ireland - an overview

Dr Dermot Power Biochemical derangements are a remarkably common finding among Emergency
Consultant Geriatrician Department attendances by elderly patients. In many instances the biochemical disturbance
St Mary's Hospital is directly responsible for the symptoms which prompted attendance and in most it is a
Phoenix Park contributory factor to the decision to admit the patient. Common causes for the biochemical
& upset include dehydration (inadvertant and secondary to diuretic use), hypo and
Mater Misericordiae hyperkalaemia (again usually caused by diuretic use) and hypercalcaemia (often representing
University Hospital underlying malignant pathology). This presentation will discuss the common causes,
Dublin consequences and management of these biochemical derangements and suggest some
methods by which the morbidity and mortality inflicted as a consequence of these disorders
of homeostasis could be avoided.



Aspects of biochemistry tests in the elderly

Ms Margaret McDonnell
Clinical Scientist
Belfast City Hospital
Northern Ireland

Population ageing has clear implications for health service planning, and for laboratory services. The number of people over 65 years has been projected to increase by 80% between now and 2025, and this means that laboratories need to review whether they are adapting to these demographic changes so that a more elderly population will have the same quality service as a younger age group.

Biochemical investigation for the elderly has perhaps greater significance for clinical diagnosis than for a younger population because of problems with multiple pathologies, nonspecific presentations of illness, difficulties with history taking, and effects of medication. Yet factors that influence how we interpret laboratory results may also be different for this population, and may mean that we misdiagnose or even overlook abnormal biochemistry results, precisely because the patient is elderly. These factors also mean that for the elderly, use of laboratory tests often has to tend towards the principles of screening rather than discretionary testing. This in itself is a particular challenge for laboratory medicine, particularly in today's climate of economic efficiency. The counter-argument, that elderly frail patients may be put needlessly through investigations must also be considered. Furthermore, we may need to examine the possibility that reference ranges and laboratory protocols that include age limits are either designed for a younger population, or are based on out-of-date estimates of life expectancy. Might we be accused of ageism?

Advances in therapeutic medicine for the elderly have also increased the focus on laboratory investigations, expanding the emphasis beyond diagnosis to include better indicators for use in preventative medicine, and in prognostic medicine. Laboratories therefore need to ensure that their tests are suitable for this special subgroup of patients, and that they are up to the challenge for this expanding population.

Management of the older person - case histories

Dr Bláithín MacMahon
Specialist Registrar in
Geriatric Medicine
St Mary's Hospital
Phoenix Park
Dublin

Electrolyte disturbances are a common problem in the elderly, and the prompt recognition and appropriate management of these abnormalities are important aspects of geriatric medicine. Principal disturbances involve both potassium and sodium. Once identified they are often easily managed. The focus of this presentation is to highlight four clinical scenarios commonly found in geriatric medicine. Our goal as physicians is to identify the disturbance, find a cause and correct the disturbance. Common aetiologies include pharmacological agents, infections and iatrogenic causes.



One foot in the Laboratory

Dr John Doran
Consultant Chemical
Pathologist
Morriston Hospital
Swansea
Wales

Population demographic changes are affecting the whole of the Western world. In the USA the 'baby boomers' are reaching retirement age with a whole change in the needs of medical care. However there is a substantial deficit in recruitment to the speciality of Geriatric medicine despite the high job satisfaction of those in the field, and while this is better on this side of the Atlantic, there is little evidence that either health systems are prepared adequately for the population changes. Already Asia has over half the world's over-65 population, and the situation in the developing world will present even greater challenges.

The role of the laboratory needs to align itself to this reality. While many illnesses are common to all the adult population, the clinical presentations and patterns of laboratory results are likely to show differences especially in the older decades. It is likely that much of the care will be by general physicians and specialists with a general interest rather than those with geriatric expertise. The laboratory needs to generate its own expertise in co-operation with the clinical geriatricians with perhaps the evolution of the 'geriatric biochemist' (but not defined by age!). With the recognition of different patterns of presentation and possible reference intervals, better advice and clinical care can be provided for the age group to which we are all heading. It's for our own personal benefit too.

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Exploring and explaining the value of the Laboratory

Dr Graham H Beastall
Department of Clinical
Biochemistry,
North Glasgow
University Hospitals,
Glasgow, UK

Recently the clinical laboratory has become more central to the healthcare system and it is widely quoted that ~70% of clinical decisions are influenced by laboratory medicine data. With this increasing importance comes responsibility. As laboratory medicine specialists we have rightly paid attention to improving the quality of the service that we deliver. In addition, however, we should see it as our responsibility to look outwards in order to add value to the service we provide.

Added value will be illustrated in four areas:

1. Improving clinical effectiveness:

Medically qualified laboratory professionals increasingly work directly with patients. The timely and intelligent combination of reporting and clinical liaison can improve clinical effectiveness and patient outcomes.

2. Adopting evidence-based laboratory medicine:

Best practice in the use of laboratory medicine services may be facilitated through evidence-based educational support to users. Appropriateness of service use, including demand management, may be stimulated through this approach.

3. Promoting the contribution of laboratory medicine to healthcare:

'Lab Tests on Line' and 'Labs Are Vital' are proving to be of great value in improving the understanding of what we do. Targeted contact with the public and patients has the same effect and can be rewarding for laboratory medicine specialists.

4. Recognising the merits of harmonisation of practice:

Variation in practice between laboratories coupled with method dependent differences can compromise patient safety and induce a loss of confidence amongst users. Acceptance of the need for harmonisation is the first step towards addressing this problem.



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 speciality area was biochemical endocrinology but more recently he has embrace evidence based medicine and best laboratory practice in primary care.

Graham has recently been elected President of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). He 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 President of the Association for Clinical Biochemistry (ACB) and currently is a member of the ACB Executive.

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 awarded the Commander of the Order of the British Empire (CBE) for services to medicine.

Session

4

On the front line Biochemistry for the emergency department

This session will critically examine the role of biochemistry tests in the emergency department.

There will be views from both a medical and laboratory perspective, including what future developments in this area may impact on the biochemistry laboratory.

Chair

Ms Geraldine Collier

Geraldine Collier has recently taken up the post as Principal Clinical Biochemist in Toxicology and TDM at Beaumont Hospital. She is a member of ACBI Council, Chair of the Republic of Ireland Region of the ACB and Chair of Biochemists Vocational Group of IMPACT. She has an interest the pathophysiology of chronic kidney disease and the use of biomarkers in the detection of CKD.

Speakers

Dr Eamonn Brazil

Eamonn Brazil qualified from UCD in 1990 and after completing his FRCSI in Ireland entered higher training in Emergency Medicine in the UK. He trained in some of the busiest academic emergency centres in England before certifying as a Fellow of the College of Emergency Medicine. He has extensive experience in all aspects of acute medicine, sports medicine and trauma. He is the Regional (Ireland) Academic Lead for Emergency Medicine for the College of Emergency Medicine (UK) and serves on several local and national emergency medicine committees. Eamonn worked in the Leicester Royal Infirmary and the Royal London Hospital before joining the Mater Misericordiae Hospital, Dublin.

Dr Danielle Freedman

Danielle Freedman is the Medical Director and Consultant Chemical Pathologist and Associate Physician in Clinical Endocrinology at the Luton and Dunstable Hospital NHS Foundation Trust. She serves on numerous RCPATH and ACB committees, both as a member and as the chair. Such committees include; chair of the RCPATH Advisory Committee for Clinical Biochemistry, chair of the ACB Clinical Excellence Awards Committee and member of UK 'Labs are Vital' Executive Board. She is also a member of the Expert Advisory Group and Guideline Development Group for NICE. She is a frequently invited international speaker on clinical cost effectiveness of laboratory medicine, clinical governance and point of care.



Clinical biochemistry - an emergency physician's viewpoint

Dr Eamonn Brazil
Consultant Emergency
Physician
Mater Misericordiae
University Hospital
Dublin

The modern emergency department requires clinical biochemistry as much as it requires radiology. In the majority of EDs, 50% or more of patients need evaluation of diverse markers of renal, liver, cardiac or respiratory function. Given that the EDs in Ireland see 1.5 million attenders annually, that means in the region of 2000 patients per day, spread unevenly through the 24 hours, and over 7 days of the week.

Much of the difficulty with the myriad of tests is a lack of understanding on the part of some users of the utility of tests, with them often being used as inappropriate filters to avoid admission, deflect from one specialty to another or even simply to look for anything abnormal when the diagnosis is obscure.

With the relatively recent introduction to clinical practice of troponin and BNP measurement, the utility of the abnormal result is at times over-estimated and the sense of security engendered by a normal result may be misplaced. Sensitivity and specificity are poorly understood by some, not alone in the training grades, leading to excessive reliance on test results to the exclusion of simple clinical common-sense. Developing tests, such as ischaemia-modified albumin will need to be validated and emergency physicians educated in their use by clinical biochemists, rather than by representatives of the manufacturers.

Increasing use of POCT enables a more rapid result to be obtained, but the limitations of the systems are often ignored by end-users. These systems require a more flexible QA and maintenance system, although it should clearly remain under the supervision of laboratory-based staff.

There is a great need for more education of end-users as to the technical aspects governing turn-around time, which remains a concern for emergency clinicians, given the urgency of some clinical presentations and the ever-present pressure on space in the ED.





Clinical biochemistry tests in A& E - what tests and knowledge is required?

Dr Danielle Freedman
Medical Director
Department of
Chemical Pathology
Luton & Dunstable
Hospital NHS Trust
Luton
England

Clinical biochemistry investigations are essential to the clinical practice of emergency medicine, both in making diagnoses and, to some extent, monitoring of disease in the acute setting. The unconscious patient (adult and child), major trauma, chest pain, shortness of breath, acute abdominal pain are some examples which are a challenge for our junior doctors for both requesting and interpreting clinical biochemistry tests.

Evidence has demonstrated that our junior doctors in England have both the lack of knowledge in what test to request and confidence in interpretation (Khromova & Gray. Ann. Clin.Biochem. 2008. 45: 33-8).

There are wide variations in test ordering suggesting that some tests are unnecessary or ordered inappropriately (E.J. Stewart et al. MJA. 2002. 177: 131-134). The role of the clinical biochemistry laboratory at both the pre and post analytical phases of investigation, including the role of clinical validation and interpretive comments, is pivotal in ensuring patient safety.

Education of users of the service should include the limitations of tests, sensitivity, specificity and predictive values. The use of clinical vignettes is an excellent teaching tool as part of an education programme for those junior doctors.

The provision of clinical biochemistry testing in A & E can, in addition, be provided by STAT laboratories and/or point of care testing (POCT). However, there is conflicting evidence that improving turnaround time of clinical biochemistry tests leads to beneficial outcomes, whether it be duration of stay in the A & E department or a reduction in length of stay in hospital. Also, as well as the clinical effectiveness of the use of POCT has to be considered, the cost effectiveness of this type of service has to be evaluated, including the resource provided by the laboratory. To implement POCT, national guidance must be followed to protect both the patient and the staff.

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- 1 Evaluation of Tosoh's G8 automated glycohaemoglobin HPLC analyzer
Lee GR, Trinick TR, Duly EB
Clinical Chemistry Laboratory, The Ulster Hospital, South Eastern Health and Social Care Trust,
Dundonald, BT16 1RH, Northern Ireland
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suppression testing
Lee GR, Johnston PC¹, McKillop D, Hunter SJ¹, Atkinson B¹, Auld PW
Department of Clinical Biochemistry and the ¹Regional Endocrine Unit, Royal Victoria Hospital,
Belfast, BT12 6BA, Northern Ireland
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Clinical Biochemistry¹ and Medical Oncology² Departments, The Mid-Western Regional Hospital,
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Kavanagh L, Kelly S, Cunningham SK
Department of Clinical Biochemistry, St. Vincent's University Hospital, Elm Park, Dublin 4
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Collier G, Greenan M, Brady J, Murray B, Cunningham SK
Department of Biochemistry and Metabolism, St. Vincent's University Hospital, Dublin
- 8 The prevalence of anaemia in patients with chronic kidney disease
Collier G, Maguire O, Cunningham SK
Department of Clinical Biochemistry, St. Vincent's University Hospital, Dublin 4
- 9 The relationship between vitamin D, parathyroid hormone (PTH) and
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Kilbane M, Houlihan G, Cannon D
Endocrinology Laboratory, Mater Misericordiae University Hospital, Dublin 7
- 10 The evaluation of the nicotine metabolite assay on the Immulite 2000
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Department of Biochemistry, Coombe Women's Hospital, Dublin 8
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 Department of Endocrinology, St. Vincent's University Hospital, Elm Park, Dublin 4 and
¹Department of Clinical Chemistry, Southend Hospital, Westcliff-on-Sea, Essex, UK
- 15** Hypernatraemia in the acute hospital setting
 McGing PG¹, MacMahon MM¹, Molloy A², Thornhill J², Redahan L², McFaul K², Wright E¹, O'Meara YM², Sadlier DM²
¹Department of Biochemistry, Mater Misericordiae University Hospital, Eccles St, Dublin 7
²Department of Renal Medicine, Mater Misericordiae University Hospital, Eccles St, Dublin 7
- 16** Evaluation and application of the novel cartilage degradation biomarker C-terminal telopeptides of type II collagen (CTX-II)
 Morrin M, Fitzgerald O, McKenna MJ, Brady J, Murray B
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- 18** AIP caused by a multigene deletion - case report and development of a PCR-based screening method
 Crowley V¹, Darby C¹, Brazil N¹, Whatley SD², Badminton M², Heggarty S³
¹Porphyria Laboratory, Biochemistry Department, St James's Hospital, Dublin 8
²Porphyria Service, UHW Cardiff and Vale NHS Trust, Wales
³QUB Genomic Core Facility, Regional Genetic Laboratory, Belfast City Hospital Northern Ireland
- 19** Prevalence of Alpha-1 Antitrypsin Deficiency in Ireland
 Carroll T, Floyd O, O'Connor C, Taggart C, Costello R, O'Neill SJ, McElvaney NG
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 Beaumont Hospital, Dublin 9, Ireland
- 20** Development of a quantitative assay to measure urinary paracetamol and 5-oxoproline to investigate the effect of paracetamol in a paediatric population
 Holmes C, Fitzsimons PE, Mayne PD
 Department of Biochemistry, Children's University Hospital, Temple Street, Dublin 1

Evaluation of Tosoh's G8 automated glycohaemoglobin HPLC analyzer

Lee GR, Trinick TR, Duly EB

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Introduction Haemoglobin A1C (HbA_{1c}) is an indicator of long term glycaemic control and its value (HbA_{1c} %) in blood correlates with the risk of microvascular disease, as reported in the Diabetes Control and Complications Trial (DCCT). HbA_{1c} is therefore measured clinically to assess glycaemic control and to monitor treatment effects in Type I + Type II diabetics. Cation-exchange HPLC is the most commonly used method for HbA1C measurement. Although current systems employ calibrators which do not exclusively contain pure HbA_{1c}, a direct comparison to the outcomes of the DCCT remains permissible.

Aim In the present study we have evaluated the G8 HPLC analyzer (Tosoh Bioscience) against our current HPLC system (ADAMS A1C HA8160, Menarini).

Methods Intra-assay and Inter-assay precision (CV) were assessed using manufacturer's IQC and pooled patient blood (EDTA) with known HbA_{1c} values between 5.5% and 10.9%. Accuracy was assessed using WEQAS distributions with known HbA_{1c} values, between 5.6% and 10.1%. Blood (EDTA) was also taken from 104 patients for HbA_{1c} measurement. Data from both analyzers were analyzed by a Spearman's rank correlation coefficient and linear regression using Excel (Microsoft) and Prism (Graphpad) software.

Results Tosoh performance:

Intra-assay precision was <0.6% (n=15-20) for IQC or patient samples whereas Inter-assay precision was <1.2% (n=10) for IQC samples. For WEQAS distributions, measured HbA1C values were 97-104% of target values.

Menarini performance:

Intra-assay precision was <1% and <0.7% (n=20) for IQC and patient samples, respectively whereas Inter-assay precision was <1.5% (n=20) for IQC samples. For WEQAS distributions, measured HbA_{1c} values were 97-101% of target values.

Regression analysis:

The correlation coefficient, slope and intercept [CI] were 0.997 [0.996-0.998], 0.997 [0.985-1.009] and 0.05 [-0.06-0.148], respectively.

Conclusion The analytical performance of the Tosoh G8 analyzer compared to the current HPLC system for the measurement of HbA_{1c} in blood supports its use in current clinical practice.

The diagnostic value of measuring nephtrines in plasma, by ELISA, in patients selected for clonidine suppression testing

Lee GR, Johnston PC¹, McKillop D, Hunter SJ¹, Atkinson B¹, Auld PW

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Introduction The diagnosis of phaeochromocytoma is complicated by its varied clinical presentation and non-specific signs and symptoms. The Clonidine Suppression Test (CST) is used to investigate patients with a strong clinical suspicion of phaeochromocytoma. A normal response to clonidine is currently given by plasma adrenaline (ADR) and noradrenaline (NAD) concentrations (mmol/L) of < 12.0 and < 3.0 mmol/L at baseline (0 minutes) and 180 minutes, respectively. Recent evidence indicates that measurement of the catecholamine metabolites metanephrine (MN) and normetanephrine (NMN) in plasma may be advantageous to the investigation of phaeochromocytoma.

Aim To evaluate the diagnostic performances of nephrine and catecholamine measurements in patients previously selected for Clonidine Suppression Testing (CST).

Methods A cohort of 67 patients was studied retrospectively. Phaeochromocytoma was confirmed by histological analysis in 14 patients and excluded in 53 patients by a negative CST, scan and clinical follow up. Plasma was used for measurements of catecholamines by HPLC and nephtrines by an ELISA. The diagnostic performance of the latter was determined by Receiver Operating Characteristic (ROC) Curve analysis. Comparisons were made to catecholamine measurements which were interpreted using current CST diagnostic criteria.

Results A sensitivity and specificity of 100% and 96%, respectively, was obtained by applying current CST diagnostic criteria to ADR + NAD measurements. Measurements of MN + NMN at baseline showed 100% sensitivity and 98% specificity as assessed by ROC curve analysis or when evaluated against published decision thresholds. A sensitivity and specificity of 100% was obtained for the combined measurements of MN + NMN at 180 minutes.

Conclusion Since HPLC analysis of plasma catecholamines is a difficult assay to perform, this study supports the use of measuring plasma nephtrines by ELISA as a more robust and equally effective test for phaeochromocytoma in patients with a high clinical suspicion.

Lead astray

O'Grady C, Palmer B, Weldon Chiu

Department of Chemical Pathology, LabPLUS, Auckland City Hospital, New Zealand

Introduction We present two cases of accidental lead poisoning.

The first occurred by self treatment using an uncontrolled "medicinal" substance. In the second, a family was affected when performing home renovations.

Lead is measured by Graphite Furnace Atomic Absorption Spectroscopy (Perkin Elmer 4110ZL with Zeeman background correction). Light absorbed at 283.3 nm from hollow cathode lamp.

Case 1 A 46 year old male presented at Emergency with abdominal pain.

Basophilic stippling seen on blood film indicated the probability of lead poisoning and a blood sample was referred for urgent analysis. Blood lead of 6.1 $\mu\text{mol/L}$ required urgent clinical intervention. The patient admitted to using a powder for local application to mouth ulcers on ten occasions. Analysis of this substance after extraction by concentrated nitric acid indicated it contained 70% w/w of lead.

Case 2 A 30 year old male was found to have an elevated lead level of 0.9 $\mu\text{mol/L}$.

In light of house renovations involving sanding of old paint, lead levels were measured on the family. Lead level on a 31 year old female was 0.5 $\mu\text{mol/L}$ while the children were much higher. A 27 month male had a lead of 1.3 $\mu\text{mol/L}$ and a 5 month male had a level of 1.9 $\mu\text{mol/L}$.

Children absorb proportionally more lead from their gastrointestinal tract than adults. Young children are most affected by lead as they may play on surfaces which contain contaminated dust, and transfer the contamination from hand to mouth. Their small body mass means tiny amounts of lead can cause poisoning.

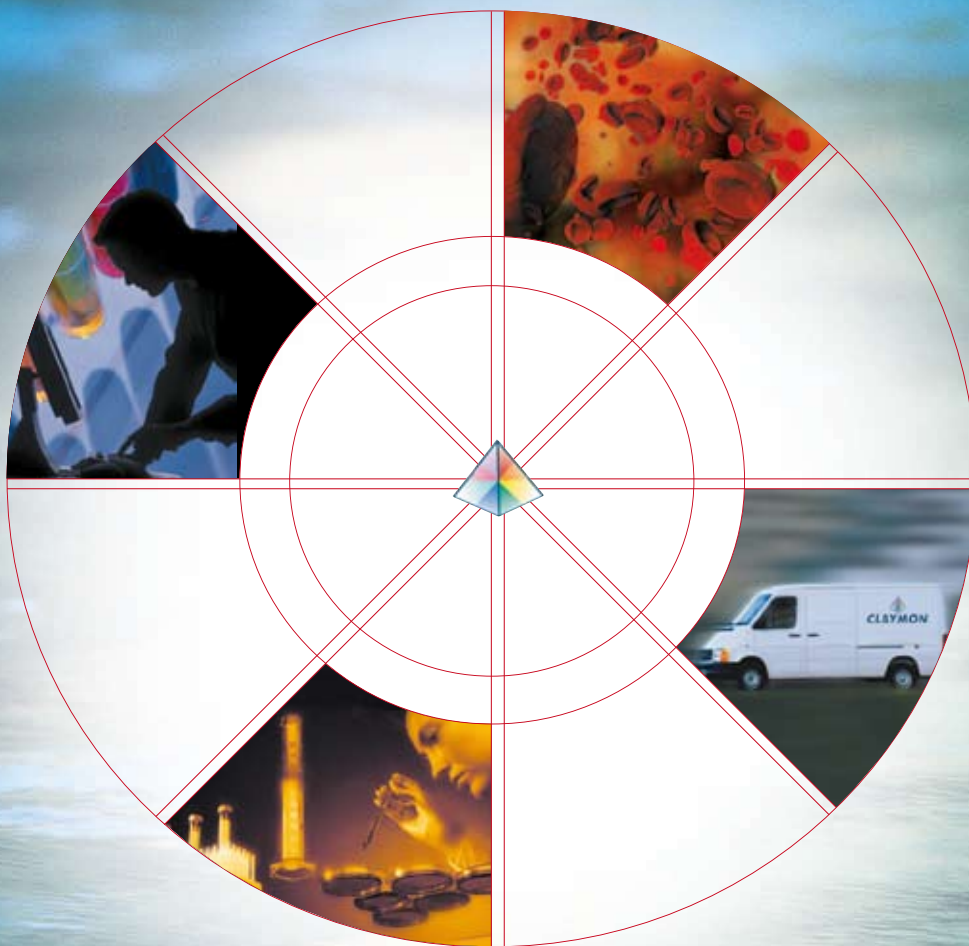
Lead poisoning following renovation is a recurring problem as more urban redevelopment of older housing areas occurs. The poisoning by use of alternative medications is an emerging problem seen in our lab and reflects the increase in the ethnic diversity in the city. These cases illustrate the need for continuing public education and awareness of the dangers of lead poisoning.





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Prolactin / Macroprolactin analysis on the Beckman Dxl

Byrne B, O'Shea P, Barrett P, Tormey W
Chemical Pathology, Beaumont Hospital, Dublin 9

Introduction Macroprolactin is a large complex containing Prolactin and usually an immunoglobulin component. Due to its large molecular mass it is confined to the vasculature and is therefore not considered to be biologically active. Commercially available Prolactin immunoassays detect Macroprolactin to variable degrees and the presence of this pseudo-hyperprolactinaemia has led to a number of misdiagnoses. As a result, guidelines have recommended that laboratories assess the reactivity of their Prolactin assay with Macroprolactin and where appropriate, introduce a Polyethylene Glycol (PEG) precipitation technique to screen for the presence of Macroprolactin.

Aims The aims of this study were:
i) to assess the Prolactin assay on the Beckman Dxl immunoanalyser and determine its reactivity with Macroprolactin
ii) to devise a laboratory protocol for the investigation of hyperprolactinaemia using the Dxl.

Methods Samples were analysed using the PEG Macroprolactin screening technique on the Wallac AutoDELFIA and the results compared with untreated samples analysed on the Beckman Dxl. Samples showing widely discordant results were analysed for a definitive result using Gel filtration chromatography (GFC).

Results The results suggest that the Dxl has a very low reactivity with Macroprolactin (1 - 2%). They also indicate that the use of the Macroprolactin screening procedure may cause a small number of genuine cases of hyperprolactinaemia to go undetected. While 1 - 2 % of samples analysed on the Dxl may have resulted in unnecessary follow up for patients, no cases of genuine hyperprolactinaemia would be missed by reporting non-PEG treated samples directly from the Dxl.

Conclusion Prolactin results should be reported directly from the Dxl without the need for PEG treatment prior to analysis. Where results do not concur with the clinical presentation, imaging studies should be considered or the sample should be re-assessed using GFC.



Unexpected serum and urine HCG concentrations in a patient with a non-trophoblastic tumour

O'Donovan M¹, Comber P¹, Barrett E¹, Gupta RK²

Clinical Biochemistry¹ and Medical Oncology² Departments, The Mid-Western Regional Hospital, Dooradoyle, Limerick

This report concerns a 36-year-old lady who presented with vaginal bleeding and pain in her lower left abdomen. Laboratory tests included a pregnancy test (negative result using Clearview; positive result using Siemens Status) and a serum HCG of 164 U/L (Siemens Immulite 2500). Investigations confirmed the presence of a locally advanced, well-differentiated squamous cell carcinoma of the cervix.

Four weeks later, the patient was admitted in preparation for treatment. The Clearview pregnancy test was negative. Treatment involved radical radiotherapy with concurrent chemotherapy. Prior to radiotherapy, the serum HCG was 372 U/L and the urine HCG was 965 U/L using the Siemens Immulite 2500. Both serum and urine HCG values were below the detection limit of the Roche Elecsys STAT assay. The pregnancy test was now positive using both the Clearview and Siemens Status products.

The patient's serum and urine HCG levels were measured on five different analytical systems. Differences in the values obtained were noteworthy. The serum HCG values were: Siemens Centaur: 117 U/L; Abbott Architect: 139 U/L; Roche Elecsys HCG+ β : 229 U/L; Roche Elecsys STAT: <1.0 U/L; Charing Cross Oncology: 211 U/L.

The urine HCG values were: Abbott Architect: 157 U/L; Roche Elecsys HCG+ β : 377 U/L; Roche Elecsys STAT: <1.0 U/L; Charing Cross Oncology: 894 U/L.

The molecular forms of HCG detected by these assay systems were: - Siemens Immulite: intact HCG, free β HCG, nicked HCG and nicked free β HCG; Roche: HCG+ β : holohormone, nicked forms of HCG, β core fragment and free β HCG; Siemens Centaur: intact HCG and free β HCG; Abbott Architect: intact HCG and β HCG; Roche STAT: holohormone only.

In the case of this patient, it appears that HCG was produced from a non-trophoblastic tumour and gave rise to unexpected serum and urine HCG concentrations. The results obtained from the six analytical systems appeared to vary with the cross-reactivity of each assay for the different molecular forms of HCG. The assay specific for the holohormone proved helpful in excluding pregnancy. Laboratories providing a service to Oncology Departments should consider having such an assay available alongside their total HCG assay.

Effects of storage temperature on the stability of common biochemistry analytes in lithium heparin gel blood collection tubes

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Introduction Non-urgent specimens that arrive at the laboratory late in the working day are centrifuged and stored overnight before analysis. Though one might intuitively store the specimens at 4°C, all stability studies by Becton Dickinson were carried out at room temperature (RT). Lithium heparin gel blood tubes are not widely used and independent data is limited.

Aims The aim of this study was to compare the analytical stability of routine chemistry analytes at initial time (t=0) and after 18h of storage overnight (ON) in lithium heparin gel tubes at RT versus 4°C.

Methods 16-paired specimens gel tubes were taken at random from routine biochemistry specimens and anonymised. They were centrifuged for 10 mins at RT at 2010 RCF. The specimens were then divided into two groups. All specimens were analysed (Roche Modular) for the following analytes at t=0: Na, K, Cl, CO₂, Urea, Creatinine, CK, Alb, bilirubin, ALP, GGT, ALT, Ca, PO₄, Mg. Group A specimens were stored at RT overnight and Group B specimens were stored at 4°C overnight. The specimens were re-analysed the following day without further centrifugation.

Results At RT a statistically significant (Wilcoxin signed rank test) decrease was observed in 3 analytes: CO₂, ALP, bilirubin and a statistically significant increase was observed in 4 analytes: K, Na, PO₄, and Alb.

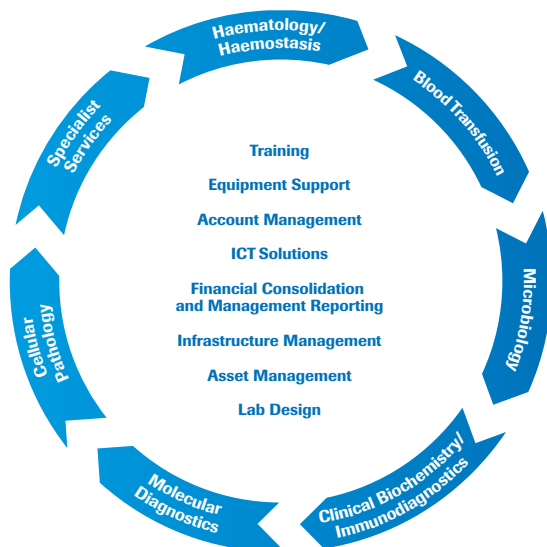
At 4°C a statistically significant decrease was observed in 7 analytes: Urea, CK, Creatinine, CO₂, Mg, bilirubin, ALB and a statistically significant increase was observed in 3 analytes: K, ALT, and PO₄

Conclusion This study demonstrates that sample storage conditions, particularly at 4°C can have a significant effect on the measurement of biochemistry analytes when stored above the gel barrier. It may be advisable to analyse samples immediately in line with BD guidelines of removal or testing of plasma from the tubes within 2h of collection. In cases where this is not possible, it may be preferable to store samples at RT.



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A study of the relationship between albumin and total protein excretion at different dipstick levels

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Aim of study To examine the relationship between total protein and albumin excretion at different levels, to assess equivalence between Albumin Creatinine Ratio (ACR) and Protein Creatinine Ratio (PCR) at the recommended cut offs for proteinuria and to calculate the sensitivity and specificity of our urine dipsticks for the detection of proteinuria.

Methods Protein Dipstick was read manually by Bayer Multistix SG, Urinary Protein and Creatinine was measured on Roche Modular and Urinary Albumin was measured by immunoturbidimetry on Roche Cobas Mira.

Results Albumin excretion correlated significantly with total protein excretion, $r = 0.965$. The Linear Regression equation: $\text{Alb} = -0.04 + 0.69(\text{TP})$; significant deviation from linearity, $p < 0.05$. As total protein excretion increases the % of albumin excretion increases. ACR correlated significantly with PCR, $r = 0.950$. Linear Regression Equation: $\text{ACR} = -4.0 + 0.68 (\text{PCR})$; significant deviation from linearity, $p < 0.01$. As PCR increases the % difference between ACR and PCR decreases.

The % albumin to total protein excretion was 22 %, 34 %, 51%, 65% and 72 % at negative, trace, +1, ++ 2, and +++ 3 dipstick respectively.

At $\geq +1$ Dipstick levels there was no discordant results between ACR and PCR.

The Bayer Multistix had a sensitivity and specificity of 98% and 82%, respectively for the detection of clinical proteinuria

Conclusions As the relationship between ACR and PCR is not linear there is no convenient conversion factor and interchange between these ratios is not recommended while monitoring a patient. We found no discordant results between ACR and PCR at Dipstick levels $\geq +1$ therefore either ratio could be used for the identification of clinical proteinuria. As the draft guidelines recommend the use of ACR there is a need to widen the analytical range in order to minimise dilutional errors which may occur. As a screening test for clinical proteinuria dipstick urinalysis had an acceptable sensitivity.

The prevalence of anaemia in patients with chronic kidney disease

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Aim of study Anaemia in patients with Chronic Kidney Disease (CKD) is a known risk factor for significant adverse patient outcomes¹. Recent data indicate that anaemia may start at a much earlier progression of CKD than previously thought². The aim of this study was to assess the prevalence of anaemia in patients under the care of the Nephrology Department in our Hospital.

Methods The prevalence of anaemia was assessed retrospectively in patients. WHO criteria was used to define anaemia, eGFR was calculated using the 4-V MDRD equation and used to stage CKD in these patients (n= 239).

Results At an eGFR > 60ml/min/1.73m², Stage 3 and Stage 4 CKD, the prevalence of anaemia in males was 33%, 32% and 88% respectively and 16%, 39% and 25% in females respectively. There was only a significant difference in the prevalence of anaemia between the sexes at Stage 4 CKD (p=0.0002).

The prevalence of anaemia significantly increased in females as renal function declined from an eGFR greater than 60 to Stage 3 CKD (p= 0.0117) but the prevalence was similar between Stage 3 and Stage 4 CKD, p = 0.45.

In males the prevalence of anaemia had a different pattern, with no significant difference between males with an eGFR > 60 mL/min/1.73m² and those with Stage 3 CKD, p = 0.262. There was a very significant difference as renal function declined from Stage 3 to Stage 4 CKD, p = 0.0004.

Discussion Very few studies have studied the prevalence of anaemia in patients with CKD, especially at lower levels of renal function. The reason why males have a large prevalence of anaemia at Stage 4 will require further investigation and other causes of anaemia, such as GI bleed, must be out ruled.

- References**
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The relationship between vitamin D, parathyroid hormone (PTH) and calcium in Irish postmenopausal women.

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The relationship between vitamin D, PTH and calcium was investigated in 82 postmenopausal Irish women. Menopause was confirmed by age and hormonal status. Vitamin D deficiency (less than 50 nmol/L) was confirmed in 32% of the subjects. However, in a subgroup with confirmed osteoporosis (DEXA scan), 60% were found to be vitamin D deficient. 13% of all subjects were identified with primary hyperparathyroidism.

When PTH levels were compared against vitamin D in all subjects, a clear relationship was seen. Declining vitamin D was seen to elicit a rise in PTH levels in these subjects. The vitamin D threshold, where a PTH response was seen, is approximately 50 nmol/L.

When vitamin D and calcium levels are compared, in the same subjects, the relationship was anomalous. This phenomenon is postulated to be due to the PTH response maintaining calcium homeostasis.

In the confirmed osteoporosis group the same vitamin D/ PTH relationship was seen, however, the vitamin D threshold for a PTH response appears to be higher.



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The evaluation of the nicotine metabolite assay on the Immulite 2000 Immunoassay Analyser and its use in urine in pregnancy

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Aims Nicotine is metabolised in the liver to cotinine, trans-3'-hydroxycotinine (the major renal excretion product of nicotine) and other metabolites and these are specific for the detection of smoking. It is intended to evaluate the Immulite 2000 Nicotine Metabolite assay and its application in urine.

Method The assay is a solid-phase competitive chemiluminescent immunoassay, linear between 10 and 500 ng/mL with an auto-dilution facility and uses a highly specific polyclonal rabbit anti-cotinine antibody.

Assay performance for precision, functional sensitivity, linearity on dilution were evaluated using control material and urine. Urine samples from 120 pregnant women in the third trimester were analysed for Nicotine Metabolite

Results Intra-assay precision at 36 ng/mL and 8506 ng/mL resulted in CV of 5.2% and 5.5% respectively (n = 10). Inter-assay precision over 20 runs resulted in CVs of 10.7% at 17.5 ng/mL, 9.9% at 53 ng/mL and 9.8% at 8975 ng/mL. Functional sensitivity investigation showed a CV of 9.4% (n=5) for a sample containing 11.7 ng/mL Nicotine Metabolite (the stated detection limit is 10ng/mL). Linearity on dilution using the automatic dilution facility; resulting in recoveries of 96-99% for the 1/100 dilution compared to the 1/40 dilution.

Urine samples from 120 pregnant women were analysed: 60 women had declared themselves as smokers and 60 as non-smokers. 32 non-smoking women had a Nicotine Metabolite of < 10ng/mL, while 28 had a value of 10-60 ng/mL. 15 of this latter group were known to have been exposed to passive smoking and their mean value was 31 ng/mL (range 12-60). The average Nicotine Metabolite value in the smokers was 5565 ng/mL with a range of 25-18891 ng/mL

Conclusion The assay performs within the manufacture's specifications for inter- and intra-assay precision. The values obtained in urine samples appear to reflect smoking status. Passive smoking results in small but measurable quantities of Nicotine Metabolite in urine.

Predictive value of thyroid peroxidase antibody positivity in subjects with subclinical hypothyroidism.

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Introduction Subclinical hypothyroidism is described as an elevated TSH between 4.0 and 10.0 mU/L in the presence of normal Free T4 and Free T3 levels. Its overall prevalence in the general population stands at between 4-10% and up to 20% in women over the age of 60 years. This group stands at an increased risk of development of overt hypothyroidism, particularly if positive for circulating Thyroid Peroxidase Antibodies (TPO.Ab).

Objectives The aim of this study was to measure the incidence of TPO.Ab positivity in an Irish patient population in the subclinical hypothyroid range as well as in the upper limit of the normal reference range (TSH 2.5 - 4.5 mU/L) and to compare prevalence against aged matched controls with TSH between 0.3 - 2.5 mU/L.

Methods The Siemens Centaur two-site Immunoassay using direct chemiluminescence was used for TPO.Ab and TSH analyses. Serum samples from 68 non-acutely ill patients were selected for comparison consisting of, Control Group (N= 20, TSH 0.3-2.5 mU/L), Intermediate Group (N = 34, TSH 2.5-4.5 mU/L), Subclinical Hypothyroidism (N = 14, TSH 4.5-10.0 mU/L).

Results A prevalence of TPO.Ab of 10% (2/20) in the control group, compared with 29.4% (10/34) and 92.8% (13/14) in the Intermediate and Subclinical Hypothyroid groups respectively ($p < 0.05$). A linear relationship between serum TSH concentration (2.5 - 10.0 mU/L) and TPO.Ab titre was evident.

Conclusion The presence of TPO.Ab is a feature of both patients with subclinical hypothyroidism (92.8%) and subjects in the upper end of the normal reference range for TSH (29%) but not for patients with a TSH in the 0.3-2.5 mU/L range. The finding of a linear relationship between TPO.Ab titre and TSH concentration in our study group may indicate that progression to subclinical disease and onto overt hypothyroidism may start within a laboratory's normal reference range. Measurement of circulating TPO.Ab in patients with TSH between 2.5-10 mU/L is a useful adjunct to frontline TFT testing to independently predict a population cohort at risk of developing future hypothyroidism.

Downward trend in the incidence of hyperphenylalaninaemia/PKU in the Republic of Ireland due to inward migration

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Introduction The Republic of Ireland has one of the highest incidences of hyperphenylalaninaemia/PKU in the west at 1 in 4500 births compared to approximately 1 in 12,000 in other western countries. This high frequency is partially due to net emigration with concentration of the gene pool and a founder effect of the most prevalent mutation R408W which has an allele frequency of 42% in the Republic of Ireland.

Since the beginning of the 20th century the annual birth rate reached a maximum of 78,000 in 1980; it then declined to 48,500 in 1994. Since then it has increased to approximately 68,000 due to returning Irish and inward migration principally from new EU accession states, Africa and Asia, all having significantly lower incidences of hyperphe/PKU than Ireland.

Method We evaluated the effect of inward migration on the incidence of hyperphe/PKU since 1980 and compared these changes with those of Congenital Hypothyroidism in which there is no significant known geographic variation in incidence.

Newborn screening for hyperphe/PKU started in 1966 using a bacterial inhibition assay until 2005 when tandem mass spectrometry was introduced. Screening for congenital hypothyroidism started in 1979 .

Results & Discussion The overall incidence of hyperphe/PKU from 1980 to 2007 was 1 in 4,400; median number of cases diagnosed per year was 13 (range 7 to 22). Between 1980 and 1985 the incidence was 1 in 3,990 (median no. cases diagnosed 17; range 12 to 22), 1990 and 1995 1 in 4,200 (median no. cases diagnoses 11; range 9 to 16) and between 2001 and 2007 1 in 5,240 (median no. cases diagnosed 11; range 9 to 18). This trend did not reach statistical significance (Mann-Whitney U test $p=0.051$). There was no comparable change in the incidence of true congenital hypothyroidism over the same time period.

Following significant inward migration since 1995 there has been a downward trend in the incidence of hyperphe/PKU in Ireland toward the European mean.

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Validation of updated software on a Laboratory Information System

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Introduction Before an updated software version of our Laboratory Information System (LIS), Isoft Apex system, was installed, testing of the new version was carried out across all disciplines in our Pathology Department. The data presented below is the validation carried out in the Clinical Biochemistry Department.

Methods The updated version was installed in a testing mode on our LIS. Demographics, tests and results entry, worksheets, report printing, rule and calculation applications, results authorization, results enquiry and sample audit trails were checked by booking in 'dummy' specimens. All interfaces were temporarily switched off in the live system and tested on the new version.

Results Testing mode:

Problems were identified in worksheets (patient details omitted), reports (specimen comments not printing) and interfaces (no communication). All problems identified were resolved prior to installing the updated software.

Post installation:

The same checks were performed and the problems identified during the testing period were not encountered- as expected. However, as a result of the increased activity associated with a live system, additional problems were identified such as calculations running slow (or not happening at all, <1%), issues with cumulative view of results, additional inaccurate entries in the sample audit trail and problems with repeat analysis of specimens.

Summary Even with comprehensive testing of updated software, it is not possible to assess it fully until it is installed in its 'running' mode in a LIS, that is, applied to a patient database and operating on a day to day basis. Realistically, only one of the problems (repeat analysis) encountered after installation of the software could have been picked up at the testing stage and this has now been included in the testing procedure for future validations. Five months after installation, the problems identified with the updated version have not been resolved as resolution requires a rewriting of software, a process which includes extensive testing before release.

Serum monomeric prolactin reference intervals determined by precipitation with polyethylene glycol: Evaluation and validation on six major immunoassay platforms

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High molecular mass forms of prolactin, primarily macroprolactin, which lack bioactivity *in vivo*, constitute a significant source of immunoassay interference and commonly result in misdiagnosis and mismanagement of hyperprolactinemic patients.

This study aimed to establish and validate reference intervals for bioactive monomeric prolactin following treatment of sera from healthy individuals with polyethylene glycol (PEG) on the predominant immunoassay platforms in routine use. Parametric reference intervals for post-PEG prolactin were derived using IFCC approved RefVal software from healthy males (n=53) and females (n=93) using the Architect (Abbott), ADVIA Centaur and Immulite 2000 (Siemens Diagnostics), Access 2 (Beckman Coulter), Elecsys 2010 (Roche Diagnostics) and AIA 1800 (Tosoh) analysers. The gel filtration chromatography (GFC) pattern of immunoreactive prolactin isoforms was also determined in normal subjects. To validate our approach we compared the classification of patients using GFC to that obtained with the newly derived post-PEG ranges.

Parametric reference intervals in mIU/L for post-PEG prolactin in male and female sera respectively were: 61-196, 66-278 (Centaur); 63-245, 75-381 (Elecsys); 70-301, 92-469 (Access); 72-229, 79-347 (Architect); 73-247, 83-383 (AIA); 78-263, 85-394 (Immulite). In normal sera subjected to GFC, monomeric prolactin comprised 30 to 85% of the total prolactin present, mean 72%. Big prolactin was a relatively constant minor component (mean 15%, range 9-23%). While the contribution of macroprolactin was more variable and ranged from 2-55%.

Concordance between GFC and immunoassay specific post-PEG reference intervals was observed in 311 out of 324 cases and for 31 of 32 patients with true hyperprolactinemia and 17 of 22 patients with macroprolactinemia. Misclassification of 5 patients with macroprolactinemia by some analysers was due to relatively minor elevations in post-PEG prolactin, mean 61mIU/L.

The availability of validated normative reference data for sera pre-treated with PEG on the most commonly used immunoassay platforms should serve to facilitate the more widespread introduction of macroprolactin screening by clinical laboratories.

Hypernatraemia in the acute hospital setting

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Background Hypernatraemia is a common clinical problem occurring in up to 1% of all hospital admissions and is associated with increased morbidity and mortality. The aim of this study was to examine the risk factors for developing hypernatremia and to identify those factors most likely to predict a worse outcome.

Methods A retrospective study of in-patients with plasma sodium greater than 150 mmol/L from the 1st January 2007 to 30th June 2008 was performed. Patients with end stage renal disease were excluded. Demographic, clinical, laboratory and outcome data were recorded. Estimated glomerular filtration rate (eGFR) was calculated by MDRD equation.

Results 150 patients who fitted the criteria above were studied. Mean serum sodium was 156 mmol/L (range 151 - 183 mmol/L), and mean age was 70 years (25 - 97 years). The commonest reasons for admission were sepsis, active malignancy and alcohol related diseases.

At the time of diagnosis of hypernatraemia, 50% of patients were managed in intensive care units while 84% of patients had active sepsis. All patients had at least one other co-morbidity - the commonest were diabetes mellitus (16.9%), advanced dementia (12.4%), and congestive cardiac failure (11.7%). Renal dysfunction was common: 40% of patients had an eGFR < 60 mL/min/1.73m² while 29% of those studied had acute renal failure at the time of diagnosis. 53% of patients with plasma sodium over 150 mmol/L died.

Conclusion Poorer outcome was associated with older age, sepsis, ICU admission and congestive cardiac failure but was not influenced by the severity of hypernatraemia, presence of ARF or dementia.



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Evaluation and application of the novel cartilage degradation biomarker C-terminal telopeptides of type II collagen (CTX-II)

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Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are forms of progressive inflammatory arthritis characterized by pain and progressive destruction of the joints. Type II collagen is the main collagen of articular cartilage and is excessively degraded in RA and PsA. Anti-TNF α therapy causes marked reduction in disease activity in both RA and PsA. During cartilage degradation, C-terminal telopeptide fragments of type II collagen (CTX-II) are released and secreted into the urine.

The aims of this study were to examine the technical performance of the urinary CTX-II assay and measure levels before and after biologic therapy.

Fasting urinary CTX-II levels were measured in patients at baseline and 1 year after treatment. Values were expressed as a ratio with urinary creatinine concentration.

A clinical index of disease activity was measured pre-treatment and 1-year post treatment using the disease activity score (DAS28). DAS28 combines information from swollen joints, tender joints, acute phase response and general health. This allows for patients to be classified as good, moderate or non-responders to treatment.

RA (n=16) and PsA (n= 11) patients with good to moderate response to treatment after 1 year had mean \pm SD baseline CTX-II values of 810.05 ± 571.48 and 477.54 ± 290.11 ng/mmol and 549.51 ± 413.87 and 299.77 ± 130.55 ng/mmol after 1 year of treatment respectively.

This novel cartilage degradation biomarker may have clinical value in monitoring response to biologic treatment and progression of disease in patients with RA and PsA.



Genetic diagnosis of hereditary hypophosphatasia in an Irish kindred

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While elevated levels of plasma alkaline phosphatase activity (ALP) are commonplace, the finding of a significantly reduced plasma ALP (hypophosphatasemia) is relatively rare. We present a case report of a patient in whom a persistently low ALP led to the diagnosis of an unusual cause for this abnormality.

The patient was a 31 year old female with a four year history of low ALP ranging from 16-21 IU/L. In addition she was noted to have elevated plasma PO₄ levels 1.49 and 1.63 mmol/L (RR 0.8-1.40 mmol/L), in the presence of normocalcaemia and normal renal function. Initial clinical and laboratory investigations ruled out various causes for her hypophosphatasemia including lab artefact, excess vitamin D, hypothyroidism, pernicious anaemia, magnesium and zinc deficiency, steroid use and bisphosphonate use. The patient had no history of bone or dental disease and a recent DEXA scan was normal. It emerged on further clinical questioning by laboratory medical staff that her 62 year old mother also had a history of low ALP, but normal plasma PO₄. On this basis it was determined that hereditary hypophosphatasia was the most likely diagnosis. While urine phosphoethanolamine (PEP) screen was negative, the history and biochemical findings indicated that an inherited defect remained likely and a genetic diagnosis was sought. A mutation scanning method using PCR amplification and direct nucleotide sequencing was developed for the entire coding region and intron-exon flanking region of ALPL, the gene for tissue non-specific ALP on Chromosome 1. A single nucleotide deletion c.1474delG (p.Ala474fs) resulting in the introduction of premature stop codon was found in both proband and her mother.

To our knowledge this is the first confirmed genetic diagnosis of adult onset hereditary hypophosphatasia in an Irish patient. In the presence of low ALP, hyperphosphataemia and/or a family history, hereditary hypophosphatasia should be strongly considered.

AIP caused by a multigene deletion - case report and development of a PCR-based screening method

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Acute Intermittent Porphyria (AIP) is due to an autosomal dominantly inherited defect of the enzyme hydroxymethylbilane synthase (HMBS), also known as PBG Deaminase, which is a key element of the haem biosynthetic pathway. The diagnosis of clinically manifest AIP is dependent on demonstrating the presence of elevated urine porphobilinogen (PBG). In either presymptomatic individuals or subjects with latent AIP genetic diagnosis is the gold standard. HMBS is located on Chromosome 11 and mutation scanning methods in routine diagnostic use have identified kindred specific mutations in HMBS in 90-95% of subjects with biochemically confirmed AIP. However 5% of subjects have no demonstrable genetic lesion in HMBS using current scanning methods.

We report an Irish kindred with clinically and biochemically confirmed AIP in whom an initial mutation scan using direct nucleotide sequencing failed to demonstrate a significant genetic lesion. It was noticed that over the vast majority of HMBS the proband and his affected son had differential homozygosity for a number of common SNPs. This suggested the possibility of a partial or total deletion of the gene. In collaboration with the Porphyria Service, Cardiff, a multigene deletion HMBS c.33+1356 to DPAGT1 c.619+702 was demonstrated using gene dosage analysis. Subsequently a PCR based method for screening was developed in the Porphyrin Lab, Biochemistry Department, St James's Hospital. This facilitated screening of further family members. Genotype phenotype correlations suggested a low PBGD activity level associated with this deletion.

This represents the first Irish kindred with a multigene deletion causing an inherited porphyria. A large deletion should be considered if there is an inability to identify a causative mutation on routine scan in subjects with a robust biochemical diagnosis of acute porphyria from a recognised laboratory, particularly if PBGD activity <50%. PCR based methods can then be applied to facilitate family screening.

Prevalence of Alpha-1 Antitrypsin Deficiency in Ireland

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Rationale AAT deficiency is a hereditary autosomal codominant disorder, resulting from mutations in the AAT gene, and classically presents with emphysema and liver disease. The most common phenotype presenting with clinical evidence of AAT deficiency is the Z phenotype, resulting in decreased levels of circulating AAT due to retention of the aberrantly folded protein in the liver. It is unclear whether the carrier status confers increased risk for disease. Demographic studies indicate that AAT deficiency is under-diagnosed and prolonged delays in diagnosis are common. World Health Organisation guidelines advocate targeted detection programmes of patients with COPD and asthma.

Methods A combination of serum AAT measurement by radial immunodiffusion (RID) or nephelometry, phenotyping by isoelectric focussing (IEF), and genotyping of DNA isolated from dried blood spot samples was used to identify AAT variants.

Results 2,000 individuals with COPD or asthma attending respiratory outpatient clinics were screened in a national targeted detection programme. A further 1,000 healthy individuals in the general population were also screened for S and Z alleles in a pilot study. The targeted programme identified 43 ZZ, 28 SZ, 7 SS, 195 MZ, 158 MS, and 6 MI individuals, as well as several other rarer phenotypes. The pilot screen of 1,000 healthy individuals identified 91 MS, 45 MZ, and a single SS case.

Conclusions The percentage of deficiency alleles detected in the targeted population was higher than anticipated from studies in other populations. The S variant, thought common to the Iberian Peninsula, was detected with unusually high frequency in both targeted and the general population. Several other rarer phenotypes were also detected. Further analysis will reveal whether these phenotypes predispose individuals to lung disease.

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Development of a quantitative assay to measure urinary paracetamol and 5-oxoproline to investigate the effect of paracetamol in a paediatric population

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Introduction Paracetamol is commonly used as an analgesic and antipyretic, however, chronic therapeutic doses of paracetamol can prove fatal. Hepatic glutathione stores are depleted when paracetamol toxicity occurs and this results in interruption of the γ -glutamyl cycle and secondary oxoprolinuria. Acquired 5-oxoprolinuria is well described in adults but less so in paediatrics. Several contributory factors include malnutrition, pregnancy, and strict vegetarian diet in adults. Acquired oxoprolinuria has also been reported in infants fed Nutramigen; in patients taking paracetamol; the anticonvulsant vigabatrin; or some antibiotics and also in patients with nephritic cystinosis. Glycine deficiency, malnutrition and other clinical conditions including sepsis all may result in depletion of glutathione and accumulation of γ -glutamylcysteine resulting excess 5-oxoproline generation and occasionally a high anion gap metabolic acidosis which sometimes precedes hepatic injury.

Aim To develop a quantitative GC/MS assay to measure paracetamol and 5-oxoproline in urine. The excretion patterns of these two metabolites were used to assess the possible toxicity of paracetamol in a cohort of patients that may be vulnerable to paracetamol toxicity.

Methods Urine from 20 paediatric patients with paracetamol detected during routine qualitative organic acid analysis and 20 patient matched controls (who were not on paracetamol and presenting with either, unexplained metabolic acidosis, liver dysfunction, on TPN/Nutramigen or with sepsis) were selected for quantitation of paracetamol and 5-oxoproline. Baseline (pre-paracetamol dose) urine, 0-2 h post therapeutic dose and 2-4 h post dose urine for each of 10 volunteers was extracted according to our in-house qualitative urinary organic acid method. Organic acid profiles were obtained after extraction with ethylacetate, conversion to trimethylsilyl derivatives, and analysis by GC/MS. A grading system was applied according to paracetamol peak height to qualitatively estimate the amount of paracetamol present in each patient and volunteer urine. For the quantitative assay ion spectra determined for each compound and an internal standard (paranitrophenol) were used to establish a SIM method. Assay linearity, precision, recovery, intra and inter-batch variation was determined. Quantitative paracetamol and 5-oxoproline ($\mu\text{mol}/\text{mmol}$ creatinine) was estimated in all patient and volunteer samples using the validated assay.

Results & Discussion Optimum excretion of therapeutic doses of paracetamol in volunteers was >4 h. Qualitative paracetamol peak heights were comparable to quantitative paracetamol results ($\mu\text{mol}/\text{mmol}$ creatinine). Results indicate that excretion levels of paracetamol and 5-oxoproline seen in selected patients appears to be greater than volunteers when corrected for urinary creatinine. Whether this finding is due to a chronic therapeutic dose, timing of urine or susceptibility in some of these patients to the prescribed paracetamol dose has to be further elucidated.



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