Proceedings of

The 28th Annual Conference

of the Association of Clinicial Biochemists in Ireland

ACBI

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WELCOME TO ACBI 2005

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ACBI 2005

The ACBI in Ireland and the World

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

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

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

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

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

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

The National Institute of Health Sciences

The ACBI Conference Brochure has been produced in association with The National Institute of Health Sciences (NIHS) in 2005.

The NIHS represents a strategic alliance between the Health Service Executive and the University of Limerick.

The primary goal of the NIHS is to advance and support high quality health related research and to promote evidence-based healthcare delivery. The approach to achieve this primary goal is through education, providing access to information, facilitating dissemination and fostering partnership between educational organisers, the healthcare service and the private sector where appropriate.

Membership of the NIHS e-library is open to all HSE Mid-Western Area employees and we encourage those with an interest in health research to access the NIHS research register at **www.nihs.ie**

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Céad Míle Fáilte

Welcome to ACBI 2005

We extend a warm welcome to ACBI members, to our distinguished speakers, to our guests, to our ACBI colleagues and to all who attend this conference.

We welcome you to the Mid-West Region and to the Riverside City of Limerick. We hope that you will enjoy the scientific and social programmes.

Our lecturers will speak on themes of importance to clinical biochemistry and indeed healthcare in general. We hope that the scientific programme and poster presentations will enhance your knowledge and understanding and contribute to your ongoing professional development.

We are grateful to the organising committees of ACBI 2003 and ACBI 2004 for help, advice and encouragement.

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

The National Institute of Health Sciences (NIHS) publishes the proceedings of the Conference in this special publication. We wish to thank Ms. Catherine Kennedy, Mr. Aidan Hickey and Ms. Aisling Nolan of the NIHS for their expert help, advice and support.

Dr. Ned Barrett (Chairman), Maire Oakley (Conference Secretary), Paula Comber, Kieran Cooper, Angela Corridan, Brian Dineen.

***ACBI 2005 Conference Committee*.**

Continuing Education

The Royal Colleges

ACBI 2005 has been approved for CME by the Royal College of Physicians of Ireland (RCPI) and for CPD by the Royal College of Pathologists (RCPath). All medical Royal Colleges in Ireland and the UK have agreed to recognise each other's approval of events.

Medical staff and clinical biochemists who have completed training and are in career grade posts and have registered for CME or CPD with one of the Royal Colleges are entitled to receive CME or CPD credits. Five credits will be awarded for each day's attendance with a maximum of 10 credits for attendance at the full conference.

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

Academy of Medical Laboratory Science

ACBI 2005 has been approved by the Academy of Medical Laboratory Science (AMLS) for the award of CPEP points. Five CPEP points will be awarded for each half-day attended or twenty CPEP points for attendance at the full conference. In order to receive these points, an AMLS member must sign the AMLS attendance register and be issued with a certificate of attendance by the meeting organiser.

Evaluation of meeting

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

Programme

Friday 14th October 2005 (Morning)

09:30 — **Registration; Tea, Coffee**

Opening Ceremony

10.45 – 10.50 — Opening Remarks: *Dr Ned Barrett, Chairman, ACBI Conference Committee*

10:50 – 11:00 — ACBI President's Address: *Dr. John O'Mullane, Cork University Hospital*

11:00 – 11:30 — Opening Lecture: *Dr. Barry McSweeney, Chief Science Adviser to the Government*

Session 1

Chairperson: Dr. Thomas Smith, St. Vincent's Hospital, Dublin

11:30 – 12:15 — The Use of Biomarkers to Study Changes in Bone Turnover
Professor Philip Jakeman, University of Limerick

12:15 – 13:00 — Androgens and the Ageing Male
Dr. Mike Wheeler, St Thomas' Hospital, London

13:00 – 14:15 — **Lunch**

Friday 14th October 2005 (Afternoon)

Sesssion 2

Chairperson: Mr. Des Kenny, Our Lady's Hospital for Sick Children, Dublin

14:15 – 15:00 — What is the Evidence Base for Biochemistry Testing?
Professor Andrea R. Horvath, University of Szeged, Hungary

15:00 – 15:45 — The Future Role of Point-of-Care Testing in Healthcare
Professor Chris Price, President, ACB, Bayer HealthCare, Tarrytown, New York, USA

15:45 – 16:15 — **Tea, Coffee**

Session 3

Chairperson: Dr. Helen Grimes, University College Hospital, Galway

16:15 – 17:00 — Age Associated Disease: The Vascular System and Ageing
Professor Declan Lyons, Mid-Western Regional Hospital and University of Limerick

17:30 — **ACBI Annual General Meeting (Members Only)**

Friday 14th October 2005 (Evening)

19:30 — **Evening meal**

21:00 — **BETWEEN WORLDS**
Irish Traditional Music on piano by Professor Mícheál Ó'Súilleabháin, World Music Centre, University of Limerick, with bodhrán and bones performance by Mel Mercier.

Programme

Saturday 15th October 2005 (Morning)

Session 4 — *Chairperson: Dr. Peadar McGing, Mater Hospital, Dublin*

9:30 – 10:15	Metabolic and Regulatory Roles of Human Adipose Tissue *Dr. Simon Coppack,* *St. Bartholomew's and The Royal London School of Medicine*
10:15 – 11:00	Common Mechanisms Underpinning Obesity, Diabetes and Cardiovascular Disease: Are There Implications for Laboratory Medicine? *Dr. Marek Dominiczak,* *Gartnavel General Hospital, Glasgow*
11:00 - 11:30	**Tea, Coffee**

Sesssion 5 — *Chairperson: Dr. Nuala McCarroll, St. James' HospitaL, Dublin*

11:30 – 12:15	Cancer in Ireland: Recent Trends *Dr. Harry Comber,* *National Cancer Registry, Ireland*
12:15 – 13:00	Palliative Medicine: An Overview *Dr. Sinead Donnelly,* *Milford Care Centre and Mid-Western Regional Hospital, Limerick*
13:00 - 14:15	**Lunch**

Saturday 15th October 2005 (Afternoon)

Session 6 — *Chairperson: Ms. Mary Stapleton, Cork University Hospital*

14:15 – 15:00	Fluid and Electrolytes: Getting the Balance Right *Dr. Peter Gosling,* *Selly Oak Hospital, Birmingham*
15:00 – 15:45	Interpretation of Thyroid Function Tests *Dr. Colin Dayan* *Bristol Royal Infirmary*
15:45 - 16:15	**Tea, Coffee**

Session 7 — *Chairperson: Ms. Paula O'Shea, Beaumont Hospital, Dublin*

16:15 – 17:00	Traceability of Free Thyroid Hormone Measurements: The Whole Truth and Nothing but the Truth? *Professor Dr. Linda Thienpont,* *University of Ghent, Belgium*

Saturday 15th October 2005 (Evening)

19:30 - 20:15	**Drinks Reception**
20:15 - Late	**Annual Dinner** Music by *'Keep in Touch'*

Speakers' Abstracts - Opening Lecture

Dr. Barry McSweeney

Chief Science Adviser to the Government

The Office of the Chief Science Adviser to the Government should be viewed in the context of the new organisational structure for Science, Technology and Innovation (STI) in Ireland incorporating the Interdepartmental Committee on STI, the Cabinet Committee on Science and Technology (S&T), the Advisory Science Council (established in 2005) and Departmental and funding agency activities. The Chief Science Adviser (CSA) will be the common link between the new Advisory Science Council, the Interdepartmental Committee and the Cabinet Committee.

Key Functions are:

- Provision of independent expert advice on any aspect of science, technology and innovation as requested by Government
- Provision of analysis and opinion on all major policy proposals being submitted to Government in the area of science, technology and innovation
- Advising on STI issues arising in the context of the EU and internationally
- Advising the Government periodically on the scale and balance of overall State investment in science, technology and innovation, having consulted with all major stakeholders
- Overseeing a system of independent evaluation of STI policy and programmes, with particular reference to cross cutting issues
- Management of the process of gathering data and intelligence, particularly in relation to R&D performance and spending

Another key task is the CSA's chairmanship of a number of groups including the Research Funders Group, a forum bringing together the Chief Executives of the research funding bodies and the head of research of those government departments not represented by the funding bodies; and the Iodine Review Group, a group to review the continued use of stable iodine as a countermeasure under the National Emergency Plan for Nuclear Accidents (NEPNA).

Speaker's Biography

Dr. Barry McSweeney

On 1 September 2004 Dr. Barry Mc Sweeney took up his position as the first Chief Science Adviser to the Irish Government. Prior to taking up this assignment, he worked for the European Commission in Brussels and Ispra, Italy, as Director General of the Joint Research Centre. He was also responsible for the development of the European Commission's Marie Curie Research Mobility Scheme.

Before leaving Ireland in 1995, he was the Director of BioResearch Ireland. He also has extensive industrial experience having worked as Director of Medical Business for Biocon Biochemicals and European Product Development Manager for American Hospital Supply.

Speakers' Abstracts - Session 1

The Use of Biomarkers to Study Changes in Bone Turnover

Professor Philip Jakeman
Human Science Research Unit, University of Limerick

Bone has traditionally been thought to maintain slow rates of turnover. Qualitative studies of turnover of bone calcium indicate a rate of approximately 1g.day^{-1} and bone collagen turnover of the order of 1-2%.day^{-1} rates that are acutely modified by environment factors such as diet and physical activity. Heaney (2003) suggests that high bone remodeling (more correctly, bone turnover, which is all that the biomarkers can estimate) makes an independent contribution to bone fragility. Heaney proposes that bone remodeling rates in ostensibly healthy people are too high; changes in nutrition and the lack of physical activity increasing remodeling inappropriately in this modern society.

It is generally agreed that the response of bone mass is too slow and too small to be useful given the time course for which feedback is required for therapeutic intervention. Biochemical markers of bone turnover provide a possible, more sensitive alternative. Debate continues as to whether markers of bone metabolism can provide adequate quantitative information to measure acute changes in bone turnover.

Experts provide guidance to clinical biochemists as to the pre-analytical and analytical procedures of measuring bone biomarkers. In this paper we present data on the analytical and biological variability of the measurement of biochemical markers of bone turnover in healthy young men and pre- and post-menopausal women. Analysed by critical difference individual variance in homeostatic levels of biomarkers representing bone formation and resorption ranged from 9.1 ± 2.6% for osteocalcin to 64 ± 35% for urinary deoxypyridinoline. Homeostatic levels of biomarkers were readily perturbed by an acute environmental intervention (physical activity) that resulted in an uncoupling of bone metabolism. Analysed on an individual basis a significant perturbation of bone turnover was observed in approximately 50% of the subjects studied. The distinct 'responder' and 'non-responder' profile identified in this study could, in part, explain the poor outcome of longitudinal studies of changes in bone mineral density.

Speaker's Biography

Professor Philip Jakeman

Professor Philip Jakeman, University of Limerick, graduated with an honours degree and research Masters Degree in Biochemistry from the University of Manchester, UK. The C.A.S.E. research scholarship award in collaboration with, the then, I.C.I. was an introduction to academia-industry partnership. A PhD at the University of Salford, completed in 1984, brought Dr. Jakeman into exercise science when, as a biochemist, he joined a multidisciplinary team to study the physiological development of athletes that including notables such as Sebastian Coe (now Lord Coe). The PhD was awarded for studies on the biochemistry of exercise under the supervision of Professor L.S. Bark, Vice-President of the Royal Society of Chemistry. Dr. Jakeman remained in Manchester to pursue post-doctoral work investigating the rate of percutaneous drug diffusion. Funded by Nicolas International these studies employed radio-labelled drug diffusion techniques to study the effectiveness of topical drug administration.

Dr. Jakeman's first appointment in the University Sector was to Manchester Metropolitan University, reaching the position of Reader before moving to the University of Birmingham in 1989. At Birmingham, Dr. Jakeman's main collaborative work was at the University's Clinical Research Unit contributing to a strong research base (HEFC rated 5 in 1996) but specialising in biochemistry and human metabolism.*

Appointed in 1995 as Professor of Exercise Science, Dr. Jakeman moved permanently to UL in 1996 as Head of Department with a responsibility to develop quality teaching and scientific research in exercise science. Released from the duties of H.O.D. and with the benefit of a sabbatical term, Professor Jakeman formed the Human Science Research Unit (HSRU) that now resides within a new suite of laboratories, commissioned in 2004, to continue his studies in human, and in particular, exercise metabolism. A collaborative base of basic and clinical scientists in Ireland assists this new venture.

Speakers' Abstracts

Androgens and the Ageing Male

Dr. Mike Wheeler

Department of Chemical Pathology, St Thomas' Hospital, London

As men are living longer and are also healthier in old age, there is more desire to be sexually active in later life. However, old age is associated with less drive, lower libido, poorer sperm quality, more erectile problems, osteoporosis and lower testosterone concentrations. Over recent years the investigation of androgen deficiency in the aged male has attracted much controversy especially as to some clinicians androgen deficiency does not mean sub-normal testosterone concentrations.

Some clinicians rely simply on testosterone concentrations to determine androgen deficiency while others state that this is an inadequate approach and rely much more on questionnaires. The latter leads to controversial testosterone replacement in men with 'normal' testosterone concentrations.

As the ageing population has grown so the interest in the health and treatment of this group has grown because of the medical, social and economic consequences. The WHO, the International Society for the Study of the Ageing Male and the Endocrine Society of America, as well as the UK Society for Androgen Deficiency have all given the subject much attention and publicity.

So is there now a clear consensus on what constitutes androgen deficiency? Are the sexual problems associated with androgen deficiency or some other mechanism that is affected by the ageing process? Are there treatable aspects of sexual dysfunction in the ageing male and how do we determine them? What role does hormone measurement play in the determination of androgen deficiency? If they are useful which hormones should be measured? This lecture will explore these issues and discuss the current arguments for hormone treatment of the aged male.

Speaker's Biography

Dr Mike Wheeler

Dr. Mike Wheeler BSc, MSc, PhD, FRCPath started with a degree in zoology and having decided this would make a good hobby then spent many an hour watching others sleep while he carried out a PhD in Renal Function during sleep. During this time he was involved in hormone investigations in manic depressive psychosis at the MRC unit for Metabolic Disturbances in Psychiatric Illness in Sheffield. More recently he was Consultant Grade Clinical Scientist and deputy head of the Clinical Chemistry Department at Guy's and St. Thomas' Hospitals. He holds an Honorary Senior Lectureship with Kings' College and is Director of the Supra Regional Assay Service for Peptide and Steroid Hormones. Dr. Wheeler is a member of several societies and associations including the UK Society for Androgen Deficiency (formerly the Andropause Society).

His specialist interest is in immunoassay development, robotics and automations and reproductive and adrenal endocrinology. His output includes over 100 peer-reviewed publications, several books and over 50 monographs on evaluation for the Medical and Health Products Regulatory Agency of the Department of Health.

Speakers' Abstracts - Session 2

What is The Evidence Base for Biochemistry Testing?

Professor Andrea Horvath

Department of Clinical Chemistry, University of Szeged, Hungary

Despite the crucial importance of the appropriate use of diagnostic tools in clinical decision-making, we fail to have sufficient high quality, valid and reliable scientific evidence in laboratory medicine to support those decisions. The causes of this paradox are manifold. Diagnostic strategies and interpretation of results should be directed by the pre-test probability of the condition and the performance characteristics of the tests, however, reliable databases on prevalence, and on diagnostic thresholds are lacking. It has also been demonstrated that the diagnostic accuracy of laboratory investigations is seriously overestimated, due to different forms of biases often related to poor study design or to the lack of appropriate gold standards. Randomised controlled trials and outcome studies in laboratory medicine are scarce, either for ethical reasons, or for the lack of methodological standards, or funding. Further concerns are publication bias, and that the results of primary diagnostic studies cannot be synthesized in systematic reviews or meta-analyses, due to heterogeneity of patient populations, the applied methods used for measurement, rapid changes in, or lack of standardisation of technologies, and changes in the definition of the disease over time.

The lack of good quality evidence in our profession not only contributes to inappropriate utilization of laboratory services but also may cause harm to patients and wastes significant resources. In order to support evidence-based best practice, the profession needs better quality

- Primary research
- Systematic reviews
- Evidence-based guideline recommendations on the use of diagnostic tests
- Knowledge management systems of critically appraised data on pre-test probability/prevalence, and the performance characteristics of laboratory tests
- Training and education about the methods of EBLM
- Better communication and dissemination of the impact of using research evidence in laboratories
- A worldwide collaboration of laboratory, clinical and methodological experts, patient organizations and the diagnostics industry in the field of EBLM.

Speaker's Biography

Professor Andrea Rita Horvath

Professor Horvath MD, PhD, EurClinChem, FRCPath (UK), is Head of Department of Clinical Chemistry at the University of Szeged in Hungary. She spent altogether 8 years in Britain, first as a scientist in London (1988-1990), later as a chemical pathologist trainee in Sheffield (1993-1994), and subsequently as lecturer in clinical biochemistry at Oxford University (1995-1998).

She has been a member (1999-2002) and since 2003 the chair of the Committee on Evidence-based Laboratory Medicine of the International Federation of Clinical Chemistry and Laboratory Medicine (http://www.ifcc.org/divisions/EMD/C-BLM/resources.asp). She is member of the advisory board of Guidelines International Network (G-I-N), and collaborates with the AGREE Collaboration. She was an international reviewer of the Evidence-based On-call Project of the Oxford Centre for Evidence Based Medicine. Since 2003 she has been a member of the executive board of CASP (Critical Appraisal Skills Programme) International. She collaborates with the Diagnosis and Screening Test Methods Group (DST-MG) of the Cochrane Collaboration (CC) and the GRADE Working Group.

Currently she is the president of the Hungarian Society of Laboratory Medicine. Since 1999 she has been a founding member of the medical laboratory sub-committee of the Hungarian Accreditation Body. In the last six years she has been active in running a national evidence-based health care programme and network, called TUDOR, in Hungary, initiated by the support of the Department for International Development (DFID) of the British Government (http://tudor.szote.u-szeged.hu). She is an advisor on EBM matters to health policy and purchasing departments of the Hungarian government and she is the leader of the Clinical Evidence Online project of the Ministry of Health's eHealth Programme.

She has published several book chapters and papers on evidence-based laboratory medicine and evidence-based guideline development and clinical audit, including the Hungarian guideline development and clinical audit manuals issued by the Ministry of Health (http://www.eum.hu/eum/eum.head.page?pid=DA_11120). She held several Central-Eastern European EBM workshops with the support of DFID, CASP International and the AGREE Collaboration and will run the first international evidence-based laboratory medicine course, together with the DST-MG of CC this fall.

Her main professional interests are evidence-based guideline development and clinical audit, evidence-based diagnosis and teaching EBM. Her hobbies are photography, skiing, canoeing and travelling.

Speakers' Abstracts - Session 2

The Future Role of Point-of-Care-Testing in Healthcare

Professor Christopher Price

Bayer HealthCare, Tarrytown, New York, USA

If point-of-care testing (POCT) is defined as "the provision of a test (result) at the point in time at which the result will be used to make a decision and take appropriate action which will result in an improved health outcome", the technology is available and the need is there. Consequently if healthcare organisations are willing and able to make the necessary changes in the way that clinical medicine is practised, then there will be an explosion in the utilisation of POCT over the next decade. The technology now exists to deliver all of the types of assays seen in much of laboratory medicine. Indeed it is probably that the application now lags woefully behind the capability – despite the need being clear.

Plans for changes in the way that health care is delivered focus on more rapid clinical decision making, shorter stay in hospital, 'one stop clinics', and devolution of more care to the primary sector. The overarching theme is patient focused, and this embraces accessibility, choice as well as empowerment. Set against these criteria the classical style of central laboratory provision of diagnostic services may be inadequate.

It is worth examining the reasons for a rapid diagnostic service. It is no longer the case that POCT is designed to meet the needs of emergency and critical care medicine. The emphasis now is about rapid decision making, rule out of diagnoses, and of therapy guidance and compliance testing - a holistic approach to a making diagnostic and therapeutic decisions in one visit to the health professional.

There is now good evidence to support these contentions, especially in the arena of the care of long term diseases such as diabetes, heart failure, anticoagulation status. There is also good data to support the use of rapid testing in the classical arenas of critical care and emergency medicine. All of these scenarios bring improved outcomes to patient and care provider.

Speaker's Biography

Professor Christopher Price, President ACB

Professor Christopher Price PhD, DSc, FRCPath, FRSC, FACB, is Vice-President of Outcomes Research for the Diagnostics Division of Bayer HealthCare. He is also Visiting Professor in Clinical Biochemistry at the University of Oxford. Prior to taking up these positions in January 2002 he was Professor of Clinical Biochemistry at the St. Bartholomew's and Royal London School of Medicine and Dentistry, and Director of Laboratory Medicine at the Barts and London NHS Trust.

Today his main professional interests lie in the area of evidence-based laboratory medicine and outcomes research, together with point-of-care testing. This not only embraces the requirement for high quality evidence to support the modern practice of laboratory medicine, but also a strong commitment to demonstrating that laboratory medicine makes a positive difference to health outcomes.

His work has resulted in over 300 publications including eight patents and the co-editing of ten books, including one on Evidence-Based Laboratory Medicine published in 2003, and another on Point-of-Care testing published in 2004, by AACC Press.

Professor Price is President of the Association of Clinical Biochemists in the UK. He has also served as a member of the American Association of Clinical Chemistry's Board of Directors.

Speakers' Abstracts - Session 3

Age Associated Disease: The Vascular System and Ageing

Professor Declan Lyons

Mid-Western Regional Hospital and University of Limerick

Age associated disease when viewed from an organ speciality perspective often appears a disparate mixture of conditions. There are emerging data to suggest that many of these conditions, e.g. osteoporosis, cognitive decline, vascular dysfunction, sacropaenia, may share a common pathogenic mechanism. The role of the vascular endothelium in the maintenance of normal cardiovascular haemostasis has been studied over the past 10-15 years. The interaction between key homeostatic systems such the arginine nitric oxide system, the sympathetic nervous system and the renin angiotensin system has also been the subject of much investigation over that time period. The role of the arginine nitric oxide system and the connections between key haemostatic systems together with abnormalities in these systems will be explored in an attempt to explain the clustering of so-called age associated disease in old age.

The most common presenting symptom in old age is the "fall". The most common cause of falls in old age is neurovascular instability e.g. orthostatic hypertension, carotid sinus syndrome. All of which are now felt to be related to combinations of endothelium dysfunction and dysfunction sympathetic nervous system. Specific age associated decline in these systems will be explored.

In addition fractures resulting from falls may in themselves have a vascular basis for their causality. The combination of postural instability with bone fragility poses unique threats to the health of older people.

There are increasing data to suggest that cognitive decline, the pathogenesis of which has been poorly understood, may in most instances also have vascular basis to it.

The age-associated response to vasculoactive drugs is, in many instances the cause of considerable morbidity and again explained by blood vessels dysfunction.

This presentation will attempt to explore the hypothesis that all of the principle age associated diseases have a common vascular pathogenic basis.

Speaker's Biography

Professor Declan Lyons

Professor Declan Lyons MSc FRCP FRCPI MD is Professor of Medical Science and Consultant Physician at the Mid-Western Regional Hospital and University of Limerick.

He graduated from UCD in 1987 and did his house jobs at the Mater Hospital in Dublin before taking an MSc in Clinical Pharmacology at the University of Aberdeen. He worked as Registrar in Medicine at Aberdeen Teaching Hospitals and took his MD thesis at The University of Aberdeen in 1992. He moved to King's College Hospital London in 1994 as Lecturer and subsequently Senior Lecturer in Medicine for Elderly and Honorary Consultant Physician. He moved to his current post in his native Limerick in 1997.

Research interests are in the areas of pharmacology of ageing and vascular pharmacology with particular clinical research interests in syncope, hypertension, nitric oxide biology, osteoporosis and osteovascular instability. Previous projects have assessed the effect of blood pressure normalisation on nitric oxide dependent vasodilatation in hypertension, the effect of ageing on nitric oxide mediated and sympathetically mediated vasoactivity, the interaction between the renin angiotensin and sympathetic nervous systems, tissue actions of ACE inhibitors and characterisation of age related vascular changes in health, hypertension and stroke. Current work has centred on the elucidation of the pathogenic mechanisms that underlie various syncopal syndromes e.g. orthostatic hypotension, variants of carotid sinus syndrome. More recently a common pathogenic relationship between bone strength, skeletal muscle activity and blood vessel function in old age (osteovascular instability) is the subject of several studies by Professor Lyons' group.

Speakers' Abstracts - Session 4

Metabolic and Regulatory Roles of Human Adipose Tissue

Dr. Simon Coppack

St. Bartholomew's and The Royal London School of Medicine

The adipose tissue mass comprises the largest organ in the body of most women and many men in Europe. The tissue has long been recognised as being important for long-term energy storage. Over the last decade there has been increasing recognition of adipose tissue's role as an endocrine organ and as a dynamic regulator or energy supply. Whether either or both of these actions contribute to the association between adiposity and insulin resistance is an area of intense research. Increasingly it is recognised that in obesity the behaviour of adipose tissue changes, but it is as yet unclear whether these changes are adaptative or maladaptive.

Although currently defined by the World Health Organisation in terms of excess weight for a given height, obesity is best considered as being an increase in adiposity. Of necessity this involves an increase in adipose tissue mass. This review will outline some of the changes in adipose tissue that occur in obesity, with especial reference to the changes in behaviour of the tissue as well as the expanded adipose tissue mass. Given that there are important differences in the way that species respond to net energy surpluses, not least in the behaviour of adipose tissue, this review will concentrate on human data when possible. There are multiple changes in adipose tissue in obesity. Energy storage in adipose tissue takes place in the post-prandial period rather than in 'basal' post-absorptive states and has been relatively little studied. There is more data about lipid mobilization from adipose tissue under conditions of fasting and exercise. There is increasing information about adipose tissue's endocrine functions. In each of these areas obesity produces abnormalities of either basal activity or responses to physiological activity (e.g. feeding/fasting) or both.

Speaker's Biography

Dr. Simon W. Coppack

Dr. Simon Coppack is Reader in Metabolic Medicine in the Academic Medical Unit at St. Bartholomew's and The Royal London School of Medicine. The post is heavily research-oriented and involves work at both The Royal London and St. Bartholomew's sites. His clinical interests (as an Honorary Consultant Physician) include obesity, lipidology and diabetes mellitus as well as general (internal) medicine.

Dr. Coppack's research interests are in the field of lipids, obesity, insulin resistance, non-insulin dependent diabetes and nutritional fluxes. He has received numerous research awards. His research has been supported by research grants from the British Heart Foundation, British Diabetic Association, The Wellcome Trust, the European Commission Biomed Framework V and others.

Dr. Coppack's publications include almost 80 peer-reviewed papers, review articles, published transactions of societies, case reports and book chapters (including Diabetes Mellitus in "Clinical Biochemistry: Metabolic and Clinical Aspects" edited by Marshall and Bangert.

Speakers' Abstracts -Session 4

Common Mechanisms Underpinning Obesity, Diabetes and Cardiovascular Disease: Are there Implications for Laboratory Medicine?

Dr. Marek Dominiczak
Clinical Biochemistry Service, North Glasgow University Hospitals Division, NHS Greater Glasgow, Gartnavel General Hospital, Glasgow G12 0YN, United Kingdom

Obesity is an emerging global health problem and a currently fashionable medical scare. It is the direct consequence of positive energy balance and results in disordered fuel storage and distribution, both dependent on the action of insulin.

Insulin action is influenced by nutrients, metabolites, and increased adipokine secretion from hypertrophic adipocytes. All contribute to the development of insulin resistance in over one third of obese individuals, mostly through interference with the intracellular signaling cascades. Insulin resistance is strongly linked to oxidative stress and to subclinical low-grade inflammation, and can itself be proinflammatory.

The most important consequence of insulin resistance is transition to diabetes that occurs in about 30% of obese individuals. Systemic inflammation accelerates this. It happens on the background of the stimulation of the fuel transport pathway, i.e. the production of the VLDL, generation of remnants and the associated decrease in HDL.

When other cardiovascular risk factors such as hypertension occur, the condition is defined as the metabolic syndrome. Metabolic syndrome spans prediabetic and diabetic states and, has a strong inflammatory component.

The common platform for the development of cardiovascular disease in obesity and diabetes is the damage to endothelium. This links into events leading to atherosclerosis known to be associated with increased LDL concentration.

Identification of fuel-distribution-related cardiovascular risk requires combined assessment of glucose tolerance and of the markers of the fuel transport pathway, plasma triglycerides and HDL-cholesterol. The low-grade systemic inflammation is assessed by the measurements of CRP. The usefulness of measurements of adipokines is still not defined.

Thus, abnormal carbohydrate metabolism caused by positive energy balance stimulates cellular mechanisms which link into the atherogenesis in a way, at least in part, different from the LDL-cholesterol-driven path. This needs to be recognized in laboratory assessment as well as in dietary and pharmacological preventive strategies.

Speaker's Biography

Dr. Marek Dominiczak

Dr. Marek Dominiczak is Consultant Clinical Biochemist at the Western Infirmary and Gartnavel General Hospital, a Senior Lecturer at the University of Glasgow, and a docent at the University of Turku, Finland. He has published over 100 papers on diabetic complications, the assessment of glycaemic control, atherosclerosis and cardiovascular prevention. In the 1990s he led two European programs of academic renewal, the first one in Poland and the second in Estonia, the former one in collaboration with Trinity College Dublin. He is an advocate of direct clinical involvement of clinical biochemists and his current clinical duties involve cardiovascular prevention and clinical leadership of the hospital Nutrition Team.

He has a major interest in medical education and publishing. He founded the Curriculum Development Committee of the IFCC and for several years he edited the journal Clinical Chemistry and Laboratory Medicine (CCLM). He is an author and editor of several books including the 'Medical Biochemistry', which is now a major undergraduate textbook worldwide.

In parallel to his commitment to clinical biochemistry, Dr Dominiczak is director of the Glasgow Medical Humanities Unit where he pursues interests in medical communication, healing environment and hospital design. He is a photographer specializing in imaging health care spaces and has exhibited his work in Glasgow and Cornwall.

Speakers' Abstracts - Session 5

Cancer in Ireland: Recent Trends

Dr. Harry Comber

National Cancer Registry, Ireland

The number of cancers diagnosed in Ireland has increased by over 3,000 cases, 16%, between 1994 and 2001. This increase is almost entirely attributable to increases in population size and average age. When corrected for these factors, the increase has been much smaller, less than 1% a year. Cancer deaths have also increased, but by only 4% over the same period, and when adjusted for population factors, the risk of dying of cancer is falling by about 1% annually.

However, this overall picture conceals major changes in trends for individual cancers. Prostate cancer numbers have almost doubled—from 1,000 in 1994 to 1,800 in 2001—and, even after correction for population changes, the risk increased by 6.5% annually, and by 21% between 1999 and 2001. The risk of renal and testicular cancers increased by 5% annually between 1994 and 2001. On the other hand, cancers of the stomach, bladder, head and neck, and larynx became much less common. Deaths from leukaemia and lymphoma are becoming more common, while mortality for cancers of the stomach, bladder, head and neck, and larynx is decreasing.

There is no single explanation for these changes—some may be more apparent than real, due to screening and improved diagnosis—but changes in risk factors, in particular smoking, diet and sun exposure, and overall prosperity, also seem to have a role.

We have also measured significant improvements in survival from most cancers, some of these associated with earlier diagnosis or increases in treatment rates, particularly in older patients, but much of the improvement has no obvious explanation. Similar improvements in survival have been seen across Europe for the past 15 years. Plausible factors include increasing sophistication of surgical and anaesthetic technique, newer chemotherapeutic agents, and, quite probably, the improving general fitness of the population.

Speaker's Biography

Dr. Harry Comber

Dr. Harry Comber has been Director of the National Cancer Registry since its establishment in 1992 and is also a part-time lecturer in Epidemiology and Public Health at University College, Cork and a member of the National Cancer Forum.

He graduated from UCC in 1971 with a BSc in chemistry and was awarded a PhD in biochemistry at the Institute of Cancer Research, London, in 1974. He then returned to UCC to study medicine, working as a clinical biochemist during holiday periods. Following a three year postgraduate training programme, he worked as a GP in west Cork, and then Cork city, until 1992. During much of this time he was heavily involved with general practice research, and was Director of the Cork General Practice Training programme from 1987 to 1992.

His major current research interest is into the impact of patient and health service factors on access to cancer services and on cancer survival, but work within the Registry, the national focus for cancer epidemiology, has involved him in a very broad range of cancer-related topics.

Speakers' Abstracts - Session 5

Palliative Medicine - An Overview

Dr. Sinéad Donnelly

Milford Care Centre and Mid-Western Regional Hospital, Limerick

Palliative Medicine is a relatively new medical specialty recognised by the Royal College of Practitioners of Ireland in 1995. Doctors in Palliative Medicine care for people who have an advanced progressive illness such as cancer. Although Palliative Medicine as a recognised medical specialty may be new, the care of people who are dying has a very long tradition in Ireland.

Having trained and worked in other countries in Palliative Medicine, i.e., the United States and Scotland, I realised the importance and wealth of tradition associated with dying and death in Ireland. Perhaps arising from this cultural richness, Ireland has led internationally in the co-ordinated development of Palliative Medicine and Palliative Care services throughout the country.

Palliative Medicine focuses on the holistic care of patients and their families. The aim is to provide an integrated service to people who have advanced progressive disease linking their care within the acute hospital, their further care in the Palliative Care Unit and their care at home. One particularly active area of development will be the integration of Palliative Care and Palliative Medicine within the acute hospital setting where most patients die.

This presentation will provide an overview of Palliative Medicine; its philosophy, service organisation, team approach to care and most importantly the manner in which holistic care is provided to patients and their families.

Speaker's Biography

Dr. Sinéad Donnelly

Dr. Sinéad Donnelly is a Consultant in Palliative Medicine in Milford Care Centre and the Mid-Western Regional Hospital, Limerick. She previously held positions in The Cleveland Clinic in the United States and Glasgow in Scotland before being appointed Consultant in Palliative Medicine in the Mid-West in 2000.

Her research interests are of a qualitative nature, developing qualitative research as a valid and reliable form of enquiry over the past five years in the Department of Palliative Medicine in Limerick. In addition Dr. Donnelly has developed a humanities programme for part of the post-graduate teaching of Palliative Medicine within the Mid-West.

She has completed a third documentary recently entitled "A Child's Grief" which explores how children deal with the death of a parent or close friend. The previous documentary, which was shown on RTE, discussed the importance of the community, e.g., neighbours and family in supporting individuals who have advanced progressive illness such as cancer at home.

Speakers' Abstracts - Session 6

Fluid and Electrolytes: Getting the Balance Right

Dr. Peter Gosling

Selly Oak Hospital, Birmingham

The commonest request in clinical biochemistry laboratories is for 'U/E' yet the understanding of fluid and electrolyte handling by those caring for the acutely ill patient is often poorly understood. Our evolved endocrine response to trauma, surgery or severe infection leads to sodium, chloride and water retention at a time when large volumes of sodium containing fluids are given to maintain the circulation and preserve tissue oxygenation retention: this risks oedema and organ failures. Sodium, chloride and water are also retained because of increased systemic vascular permeability to plasma proteins, especially albumin, which sequesters fluid in the interstitial space and also causes oedema.

Excessive fluid and electrolyte retention and interstitial oedema are associated with the systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction and failure. In this presentation I will try to give an overview of these processes and address the question, 'Can manipulation of fluid resuscitation influence the inflammatory response to trauma or surgery?' Results of randomised controlled prospective clinical studies suggest that limiting the sodium and chloride input and optimal use of synthetic colloids, which are well retained in the vascular space, can reduce the inflammatory response to injury and improve organ function. This is an area of medicine where the clinical biochemist can make a significant contribution.

Speaker's Biography

Dr. Peter Gosling

Dr. Peter Gosling BSc MSc PhD FRCPath ABSM is a Consultant Clinical Scientist at University Hospital Birmingham and honorary senior clinical lecturer at the University of Birmingham. He originally studied Medical Biochemistry at Birmingham University and music at Birmingham Conservatoire and followed this with a PhD in metabolic bone disease in patients with renal failure.

In 1984 he was appointed to Principal Biochemist with a special interest in trauma and burns and worked closely with Birmingham Accident Hospital. It was there that he discovered the association between acute inflammatory stimuli leading to increased capillary permeability and low level proteinuria.

His research interests have since broadened and include investigating the pathogenesis of multiple organ failure in the critically ill and optimizing fluid resuscitation. He has published over 100 original papers and reviews in this and related fields. ICU medical and nursing staff indulge his daily visits to the intensive care units, where he attempts to match laboratory data with clinical changes at the bedside.

Speakers' Abstracts - Session 6

Interpretation of Thyroid Function Tests

Dr. Colin M. Dayan

Bristol Royal Infirmary and University of Bristol

Routine clinical biochemistry laboratories typically perform in excess of 50,000 thyroid function tests per annum.

Although the interpretation of the majority of tests is straightforward, there remain a minority that present a challenge. Here we discuss the seven different patterns of thyroid function tests results, along with their common and rare causes.

It is proposed that in difficult cases, all three tests (TSH, free T4 and free T3) are required and where all 3 results are within the reference range the patient can be confidently assumed to be euthyroid.

Unusual cases are discussed, along with the role of thyroid function tests in thyroid eye disease, goitre and in patients on thyroid hormone replacement, and recent revisions to the "normal" range for TSH as well as the prevalence of thyroid dysfunction in the general population.

Speaker's Biography

Dr. Colin Dayan

Dr. Colin Dayan trained in medicine at University College, Oxford, Guy's and Charing Cross Hospitals before studying for a PhD in the cellular immunology of autoimmune thyroid disease with Marc Feldmann. He then spent a year as an endocrine fellow at the Massachussetts General Hospital in Boston, USA on a Harkness Fellowship before completing his specialist training in diabetes and endocrinology as a Lecturer in Bristol. He has been a consultant senior lecturer in medicine at the University of Bristol since 1995, and Head of Clinical Research at the Henry Wellcome Laboratories for Integrated Neuroscience and Endocrinology since 2002. In 2003 he received a PPP mid-career award to study the design and analysis of clinical trials. Since that time, his research has evolved from basic immunology to clinical research in thyroid disease, steroid resistance and close collaboration with Prof Mark Peakman at King's College London to develop a vaccine for Type 1 diabetes. He leads the diabetes service at Bristol Royal Infirmary, and plays a key role in the insulin pump service and the islet transplant programme in Bristol. Dr Dayan has a particular interest in collaboration between primary and secondary care in diabetes management and also runs a joint thyroid eye disease clinic. He is chairman of the Thyroid Eye Disease Charitable Trust.

Speakers' Abstracts - Session 7

Traceability of Free Thyroid Hormone Measurements: The Whole Truth and Nothing but the Truth?

Professor Dr. Linda Thienpont
Laboratory for Analytical Chemistry, Faculty of Pharmaceutical Sciences, Ghent University, Belgium

The metrological traceability of serum free thyroid hormone (FTH) measurements has until now not been achieved. This would require trueness-based reference measurement procedures (RMPs) capable of measurement of the 'true' hormone concentration in 'serum water'. Currently, no analytical principle is capable of doing so 'directly' in serum. All RMPs proposed so far (equilibrium dialysis (ED), ultrafiltration (UF)) require separation of serum water from serum. However, it is unknown whether separation can be achieved without altering the serum free/protein bound equilibrium. In this context, a European project investigated the following work hypothesis: if it can be shown that UF and ED produce 'serum water' with identical thyroid hormone concentrations, one can infer that the serum water they generated is the 'true' water fraction present in serum (1). The experiments showed that with UF procedure-dependent results were obtained and that the UF and ED results differ. In other words, currently, trueness-based traceability of FTH measurement cannot be established and other approaches to traceability (standardisation) will have to be used, e.g., traceability to a standard measurement procedure or reference materials with value transfer (2). In case of the selection of an UF or ED based standard procedure, detailed prescription of the devices and conditions will be required (3). Meanwhile, the European project opted for ED coupled to isotope dilution-liquid chromatography-mass spectrometry (ID-LC/MS) measurement of the hormone concentration in the dialysate. Reference materials could be carefully pooled hypo-, eu-, and hyperthyroid sera to which 'reasonable values' are assigned, e.g., the mean as obtained by currently existing assays or values provided by ID-LC/MS after ED. However, even after establishing a traceability basis for FTH measurements, more accessible techniques such as symmetric dialysis (4) will remain of utmost importance in assessing the specificity of routine assays for measurement of challenging clinical specimens via split-sample method comparison.

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Speaker's Biography

Professor Dr. Linda Thienpont

Studies:

University of Ghent (Belgium), Faculty of Pharmaceutical Sciences

- *1976: Pharmacist*
- *1981: Ph.D.*
- *1984: Clinical Chemist*
- *1989: Second Ph.D. in bio-analysis*

Current position:

Director of the Laboratory for Analytical Chemistry at the Ghent University.

Teaching assignments:

- *Instrumental Analytical Chemistry (Bachelor in Pharmaceutical Sciences)*
- *Development and Validation of Analytical Methods (Master in Pharmaceutical Sciences)*
- *Statistics and Quality Control (Clinical Chemist Education).*

Main scientific interest: Standardization in Clinical Chemistry

- *Development and validation of reference measurement procedures for electrolytes, substrates, steroid hormones, thyroid hormones, peptides and proteins using ion chromatography, isotope dilution-gas chromatography/mass spectrometry and electrospray liquid chromatography/mass spectrometry*
- *Statistical and graphical techniques for validation of routine test systems by method comparison with reference measurement procedures*
- *Application of reference measurement procedures for certification of serum panels to be used by industry and EQA-organizers for validation/demonstration of metrologic traceability*

In this particular field she has over 60 publications and took/takes part in the following scientific activities, projects and events:

- *Certification of reference materials for the BCR and IRMM (Commission of the European Communities)*
- *Chair of the "European External Quality Assessment Scheme (EQAS) Organizers Working Group on Reference Methods and Materials" (1992-1996)*
- *Delegated member for Belgium in CEN/TC 140 "In vitro diagnostic medical devices" mandated with EN ISO 17511 standard*
- *Chairperson of the "IFCC Working Group on Standardization of Cortisol Measurements"*

Speaker's Biography

Professor Dr. Linda Thienpont is also a:

- *Member of the "Network of Reference Laboratories" established in the framework of "IFCC Project for Standardization of HbA_{1C} Measurements"*
- *Scientific member, delegated by IFCC, in the "Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) Area Committee on Clinical Chemistry and Toxicology"*
- *Chairholder of the "CLSI Subcommittee for Free Thyroid Hormone Measurements"*
- *Scientific member of the "CLSI Subcommittee on Expression of Uncertainty of Measurement in Laboratory Medicine"*
- *Scientific member of the "CLSI Subcommittee on Validation and Implementation of Secondary Reference Materials"*
- *Co-chair of "WG#2 of the Joint Committee on Traceability in Laboratory Medicine (JCTLM)" [BIPM - IFCC]*
- *Scientific member of the "IFCC Committee on Traceability in Laboratory Medicine"*
- *Chairperson of the "IFCC SD-Working Group on Standardization of Thyroid Function Tests"*

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Poster 1

Title: An Audit of Glucose Tolerance Tests (GTTs)

Authors: McGing, P.,[1] Wright, E.,[1] Al-Agha, R.,[2] Kinsley, B.,[2] Kyne, F.[1]

Address: Biochemistry Department[1] and Department of Diabetes and Endocrinology[2]
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Introduction

For many patients the 2-hour GTT is a very important aspect of the diagnosis, or exclusion, of diabetes mellitus or other impairment of glucose homeostasis. However the test is not without controversies. We carried out an audit of GTTs performed in this hospital during 2004.

Methodology

Results of all GTTs performed in MMUH Biochemistry Department during 2004 (n=736) were extracted from the laboratory information system. Our GTT protocol involves giving 75g anhydrous glucose as 394ml Lucozade. Results were classified as normal (N), impaired glucose tolerance (IGT), impaired fasting glucose (IFG) or diabetes mellitus (DM) according to standard WHO criteria.

Results

a) Overall, approximately one-third of GTTs fell into each of the following groups: Normal (34.0%), DM (31.1%), and impaired glucose (34.9%; comprising IFG=9.5%, IGT=25.4%).

b) Of 411 GTTs where the fasting glucose was normal (<6.1 mM), in 250 (60.8%) of these cases the 2hr post-glucose sample was also normal. However in 125 cases (30.4%) the 2hr sample indicated IGT and in 36 cases (8.8%) diabetes would be the diagnosis (subject to repeat finding on two occasions).

c) Although one expects the 2hr result to be higher than fasting, this does not seem to be always the case. We found 2hr Glu < F Glu in 123 of the GTTs, comprising 16.7%. This agrees with other recent abstracts. Interestingly this group (2hr<F) had lower mean age (54.4 years) versus those with F<2hrs (63.1years) (t-test: p<0.001).

Conclusion

This audit demonstrates that the idea proposed in some centres of using normal fasting glucose to out-rule glucose abnormalities is untenable – in this study nearly 40% of those with F Glu<6.1 had an indication of IGT or DM. Our finding of lower 2hr glucose requires further investigation.

Poster 2

Title: Audit of Standards of Diabetes Care in a Hospital Out-Patient Setting Against the Standards of the New GP Contract

Authors: Ryan, M., Tracey, F., Diong, K.L., Glass, M., Curry, J., McKenna, O.

Address: Causeway Hospital Diabetes Team, Coleraine, Northern Ireland

Introduction

The introduction of the new GP contract in Great Britain and Northern Ireland in 2004 has led to significant changes in practice and emphasis in relation to the care of patients with diabetes. The linkage of remuneration to achievement of specific targets has resulted in a new focus on biochemical monitoring and quantifiable end-points. The adoption of these targets in primary care provides an opportunity to compare directly the quality of care provided in primary and secondary care clinics.

Methodology

Over the 2004-'05 audit period 769 patients have been identified as attending the clinic. Patient demographics and clinical details (e.g. body mass index, blood pressure, smoking status) and biochemical parameters (e.g. lipids, HbA_{1c}) were taken from the clinic database by independent auditors. Details were compared with treatment targets set out for primary care in the current GP-contract in Northern Ireland. The contract awards points for reaching set targets, e.g. 11 points for achieving 85% of patients having a HbA_{1c} < 10%. The points are linked to % of target achieved and the total points achieved are linked with remuneration of the practice by the Health Board for diabetes care.

Results

The Hospital-based clinic achieved 85% of total available points. The loss of 12 points for HbA_{1c}<7.4% may be due to the fact that the patients seen at the hospital clinic are more likely to be complex cases and more advanced in the natural history of diabetes, or that patients who have higher HbA_{1c} are referred preferentially from primary care.

Conclusion

Alternatively, either the standards set for primary care are too high or the quality of care provided in the hospital clinic is unsatisfactory in relation to HbA_{1c} control.

Poster 3

Title: Seven Year Outcome of Weight Loss/Exercise Promotion in a Diabetes Out-Patients Service

Authors: Ryan, M., Tracey, F., Diong, K.L., Glass, M., Curry, J., McKenna, O.

Address: Causeway Hospital Diabetes Team, Coleraine, Northern Ireland

Introduction

Weight control is an important aspect of the management of the patient with diabetes. With the exception of metformin, oral agents and insulin promote weight gain. A conflict can arise in practice with the desire to achieve optimal glycaemic control and avoid weight gain. Many studies have confirmed that weight gain is almost inevitable, particularly in Type 2 diabetic patients and weight gain is accepted as a price worth paying to achieve glycaemic control through the early use of insulin in Type 2 diabetic patients.

Objective

We decided in 1997 to adopt a deliberate policy of actively promoting weight loss through diet, weight reducing agents, and exercise, as a means of improving glycaemic control without recourse to weight promoting agents such as insulin and sulphonylureas.

Methodology

256 patients have been identified as attending the clinic over the 7 year audit period 1997-'98 to 2004-'05. Details were compared with standard treatment targets and with the UKPDS 15-year follow-up data.

Results

Average BMI was maintained at 30 in Type 2 patients and increased from 28 to 29 in Type 1 patients over the 7 years of follow-up. This compares favourably to the UKPDS intensive treated cohort which gained 6kg in weight over 7 years. Average HbA_{1c} increased in Type 2 diabetics from 8.5% in 1997-'98 to 8.9% in 2004-'05.

Conclusion

Weight gain can be minimised in diabetic patients by appropriate treatment choices, follow-up, and education without significant impairment of glycaemic control. Active promotion of weight loss and exercise can be successful in maintaining weight in both Type 1 and Type 2 diabetic patients over many years.

Poster 4

Title: The Effect of Serum Creatinine Method Choice on the eGFR Determined by the Abbreviated MDRD Formula

Authors: McKillop D.J.,[1] Cairns B.,[1] Duly E.,[2] Ryan M.F.[3]

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Introduction

The UK Chronic Kidney Disease guidelines have recently recommended the use of the abbreviated Modified Diet and Renal Disease (MDRD) formula for the routine estimation of GFR (eGFR) on each serum creatinine request.

Objective

The aim of this study was to establish the influence variation in serum creatinine between methods used by laboratories within Northern Ireland would have on the eGFR calculated by the abbreviated MDRD equation.

Methodology

Fifty patient samples were analysed for serum creatinine by the compensated kinetic assay on the Roche modular instrument and the kinetic assays on the Beckman and Abbott platforms. Method comparison of creatinine and eGFR obtained by the Roche and Abbott methods vs. the Beckman method used in the derivation of MDRD equation, were preformed by Passing-Bablok regression analysis.

Results

The median (inter-quartile range) for serum creatinine concentrations were 130 (96 – 189) µmol/L by Beckman assay, 115 (87 – 172) µmol/L by Roche assay, 120 (88.5 – 173) µmol/L by Abbott assay. The regression equation for serum creatinine were as follows: - Beckman vs. Roche: y=0.942x – (-5.6), correlation coefficient r=0.999, P<0.0001, Beckman vs. Abbott: y=0.882x - 4.5, correlation coefficient r=0.999, P>0.0001, Abbott vs. Roche: y=0.935x – 10.4, correlation coefficient r=0.999, P>0.0001.The median (inter-quartile range) eGFR calculated by the abbreviated MDRD equation were 45.4 (31.7-66.6) ml/min/1.73m^2 for Beckman Kinetic assay, 49.2 (35.4 – 78.1) ml/min/1.73m^2 for Roche compensated assay, 50.0 (35.1-71.2) ml/min/1.73m^2 for Abbott kinetic assay.

Conclusion

Alternative methods for creatinine determination used by laboratories in Northern Ireland introduces a positive systemic bias of ≈10%, the clinical significance of which will have to be considered by those tasked with the introduction of eGFR in the region. The equation of the line reported in this study could if deemed necessary be used to align the methods.

Poster 5

Title: The Clinical Impact of Introducing the Measurement of the Albumin Creatinine Ratio

Authors: Brady, J.J.,[1] Murray, B.F.,[1] McKenna, T.J.[2]

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Introduction

Urine albumin concentration is an independent predictor of microvascular disease in diabetic patients, and can alter the course of preventative treatment. Although the albumin excretion rate (AER) is considered the 'gold standard' for measuring albumin concentration, the UK guidelines on diabetes management recommend the measurement of albumin creatinine ratio (ACR) as an appropriate screening test.

Methodology

Following the introduction of ACR measurement we assessed a) the albumin requests received, and b) the sensitivity of urine dipstick analysis compared to laboratory measurement of albumin. Over a one month period 224 urine samples were received, 151 (67%) for ACR and 73 (33%) for AER. All samples were tested for protein by dipstick and albumin by immunoturbidimetric assay.

Results

- Raised ACRs were found in 23 (15%) samples, 12 of which had not been detected previously. The remaining 11 agreed with previous AER results.
- A raised AER was detected in 11 (15%) samples, 7 of which had not been detected previously.
- 100 (66%) of the ACR samples had a negative dipstick and normal urine ACR (<2.5µg/mmol).
- 28 (18%) had a negative dipstick but were classified as microalbuminuric (2.5-25µg/mmol). Of these, 14 were considered elevated due to abnormally low creatinine concentration.
- 52 (71%) AER samples had a negative dipstick and a normal AER (<20µg/min).
- 10 (13%) AER samples had a negative dipstick but with results in the microalbuminuric range (20-200µg/min).

Conclusion

Requests for ACR have increased the albumin workload by 30% since its introduction. Agreement between ACR and AER is good and sample collection is convenient. Laboratory measurement of urine albumin concentration is more sensitive than dipstick analysis for the early identification of patients who may develop diabetic nephropathy at a later stage.

Poster 6

Title: A Study of Aqueous Humour Levels of Ascorbate and Uric Acid in Patients Undergoing Cataract Surgery

Authors: Firth, G., Firth, M., Karim, A., Collins, C., Thompson, G.

Address: Princess Royal Hospital, Sussex, UK and The Eye Research Unit, St. George's Hospital, London, UK

Introduction

Antioxidants are thought to play a role in the aetiology of cataract disease. High levels of both ascorbic acid and uric acid are found in the aqueous humour of the eye and these may have antioxidant effects and/or provide protection against UV damage. Ascorbic acid levels in these patients have been studied extensively however there is little information in the literature on the levels of uric acid in the aqueous humour of cataract patients.

Methodology

250 patients undergoing cataract surgery at St. George's Hospital were recruited into the study following informed consent. A food questionnaire was completed prior to surgery and blood and aqueous humour was collected at surgery for measurement of antioxidants by HPLC with electrochemical detection.

Results

Mean concentrations of ascorbate in the aqueous humour and plasma were 1.42 and 0.039 mmol/L respectively. Uric acid concentrations were 0.097 and 0.35 mmol/L respectively. There was a weak inverse correlation between the ascorbate and uric acid levels in the aqueous humour but not in plasma. There was a weak positive correlation between the ascorbate intake as assessed by food questionnaire and the plasma ascorbate level but no correlation with aqueous humour ascorbate levels.

Conclusion

Significant concentrations of uric acid are found in the aqueous humour. Whether or not it has an antioxidant role in cataract disease is the subject of further study. Aqueous levels of ascorbate are relatively independent of ascorbate intake with little increase in aqueous levels (and presumably therefore of antioxidant activity) once a relatively low threshold of ascorbate intake has been achieved.

Poster 7

Title: Are Single Measurements of Antioxidant Activity in the Aqueous Humour of the Eye Meaningful?

Authors: Firth, G., Firth, M., Karim, A., Collins, C., Thompson, G.

Address: Princess Royal Hospital, Sussex, UK and The Eye Research Unit, St. George's Hospital, London, UK

Introduction

Antioxidants are thought to play a role in the aetiology of cataract disease. High levels of both ascorbic acid and uric acid are found in the aqueous humour of the eye. It is not known to what extent these concentrations fluctuate over time and therefore it is difficult to gauge the significance of assays of single samples taken at the time of cataract surgery.

Methodology

As part of a larger study involving 250 individuals, 16 patients underwent cataract surgery on their second eye in the same unit and under the same surgeon (GT) as for the first. Blood and aqueous humour ascorbate and uric acid were measured on both occasions and many patients completed a second food questionnaire. Ascorbate and uric acid levels were measured by HPLC with electrochemical detection.

Results

There was a high correlation between the ascorbate (R=0.84) and uric acid levels (R=0.77) of the first and second eye for each patient even though the time interval between operations was up to 12 months. The results of the food questionnaires (n=12) were also highly correlated for most patients (R=0.6 or 0.94 after removal of two outliers). For the small number where a significant difference was found it was not possible to determine whether this was due to seasonal variation or the impact of changing health or vision during the interval between the two operations.

Conclusions

Aqueous humour levels of ascorbate and uric acid remain relatively unchanged over periods of up to 12 months in most cataract patients indicating that single point measurements of these antioxidants in the aqueous humour is probably a valid measure of that individual's aqueous humour antioxidant status.

Poster 8

Title: *In vivo* Assessment of Retinal Antioxidant Status and the Risk for Age Related Macular Degeneration (AMD)

Authors: O'Donovan, O.,[1] Beatty, S.,[1,2] Nolan, J.[1]

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Department of Ophthalmology, Waterford Regional Hospital, Ireland[2]

Introduction

Macular pigment (MP) is composed of two hydroxycarotenoids, lutein (L) and zeaxanthin (Z), and is entirely of dietary origin (1). There is a growing body of observational evidence in support of the hypothesis that macular pigment (MP) protects against age-related macular degeneration (AMD), as it is known to be an effective blue light filter, and powerful antioxidant within the retina (2). There exists a consensus that dietary intake of L and/or Z represents one of the most important determinants of MP optical density, consistent with cross-sectional and supplementation studies (3). However, various factors have been observed to affect serum L (and Z) and/or MP optical density, and these include: age; gender; body fat; ultraviolet light exposure; smoking and drinking habits (4).

Objectives

This study was undertaken to investigate the relationship between MP optical density, serum L and Z, and dietary intake of L and Z in healthy subjects, and to relate these measures to putative risk for AMD.

Methodology

Four hundred healthy subjects aged between 20 and 60 years volunteered to participate in this study. MP optical density was measured psychophysically using heterochromatic flicker photometry (HFP), serum L and Z were quantified using RP-C18 HPLC, and dietary intake of L and Z was assessed using a validated Food Frequency Questionnaire. Clinical and personal details were also recorded, with particular attention directed towards putative risk factors for AMD.

Results

Dietary L and Z showed a positive [r = 0.211 and 0.234] and significant [$p < 0.01$] relationship with MP optical density. Serum L and Z also demonstrated a positive [r = 0.171 and 0.139] and significant [$p < 0.01$] relationship with MP optical density. Subjects with a confirmed family history of AMD had significantly lower MP optical density than subjects with no known family history of the disease [0.244 vs. 0.307; $p < 0.05$], and smokers also had a relative lack of MP [0.241 versus 0.308; p = 0.056]. Females had significantly lower MP than males [0.269 vs. 0.346; $p < 0.01$], and age was inversely related to MP optical density [r = - 0.256; $p < 0.01$].

Conclusions

There was a significant and positive relationship between dietary intake of L and Z and MP optical density; diet and serum levels of L and Z; and serum levels of L and Z and MP optical density.
In the absence of retinal pathology, the relative lack of MP among smokers, females, and subjects with a confirmed family history of ARM supports the hypothesis that the macular carotenoids may be protective for ARM.

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Poster 9

Title: Evaluation of the Ischemia Technologies Ischaemia Modified Albumin (IMA) Assay on the Beckman Coulter LX-20

Authors: Maguire, O., O'Sullivan, J., Collier, G., Ryan, J., Cunningham, S.K.

Address: Clinical Biochemistry Department, St Vincent's University Hospital, Dublin 4, Ireland

Introduction

Ischaemia modified albumin (IMA) is albumin in which the n-terminal is either damaged or bound to copper. When albumin circulating in blood comes in contact with ischaemic myocardium, some of it is converted to IMA. Kinetic studies have shown that IMA rises within minutes of an ischaemic event and returns to baseline six hours after cessation of ischaemia. IMA is unable to bind transitional metals and the Albumin Cobalt Binding (ACB) test measures the cobalt binding capacity of albumin to determine IMA levels in serum. IMA results, in conjunction with cardiac Troponin analysis and ECG may help in the management of patients presenting to A/E with chest pain.

Methodology

The IMA (ACB) Test (Ischemia Technologies) was evaluated on the Beckman Coulter LX-20.

Results

The within-batch CV's (n=20) on fresh patient sera at 88 U/ml, 99 U/ml and 120 U/ml were 1.4%, 2.0% and 2.5% respectively. The between batch CV's on quality control material at 74 U/ml (n=41), 84 U/ml (n=46) and 123 U/ml (n=47) were 3.4%, 3.3% and 3.0% respectively. Comparison with a reference instrument (Cobas Mira Plus) yielded the following linear regression equation; y (LX20) = 0.86 (Cobas) + 10.79; r^2 =0.99. IMA values increased in serum by an average of 10% when stored at 4ºC for 5 to 24 hours. Our laboratory established its own reference range on a population of 81 healthy subjects (28 males, 53 females, age range 22 – 86 years). The upper 97.5 percentile was 110 U/ml, significantly higher than that quoted by the test manufacturer (85 U/ml).

Conclusion

In summary, the IMA assay was found to have acceptable precision, accuracy and performed very satisfactorily on the LX-20. However, the instability of IMA (samples have to be either analysed or frozen within two and an half hours of draw) may impact on its routine use. In addition, further studies are required to assess the role of IMA as a useful marker of myocardial ischaemia.

Poster 10

Title: A Comparative Study between Total Iron Binding Capacity Measured Chemically and Derived from Transferrin Levels on Beckman LX-20 Pro

Authors: Collier, G., Maguire, O., Reece, R., Cunningham, S.K.

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Introduction

Determination of Transferrin offers a new alternative for assessing Total Iron Binding Capacity (TIBC) in serum.

Objective

Our aim was to compare a derived TIBC from transferrin with measured TIBC and also to investigate the effects of ferritin and albumin concentrations on both methods.

Methodology

Results were evaluated on 80 patients under investigation for iron status. Iron, measured TIBCm and albumin were analysed by chemical means and transferrin by immunoturbidimetry on a Beckman LX-20 Pro instrument. TIBCc was derived from transferrin results. Ferritin was measured by immunoassay on DPC Immulite.

Results

Transferrin results gave the following Passing and Bablok method conversion equation: TIBCc=22 x transferrin (g/L) + 5.8. This closely agrees with theoretical factor of 25 - the factor we then used to calculate TIBC. TIBC values obtained ranged from 16-105 umol/L.TIBC results were then evaluated according to ferritin levels: At ferritin concentrations <1000 ug/L, there was excellent agreement between both TIBC methods, with less than 1.0% difference; t=0.23 (0.05 critical t=1.9).However, in 27 patients with ferritin levels > 1000 ug/L, higher TIBCm values were obtained compared to TIBCc and the difference (10%) appeared to be directly proportional to the ferritin level; t= 3.06 (0.05 critical t=1.9).In 2 patients discordant transferrin saturation levels were obtained at our cut-off for screening for iron overload (45%). There was no significant difference between TIBC methods when albumin concentrations were in the range 10-46 g/L.

Conclusion

The determination of TIBC by calculation from transferrin is precise, robust, cost effective and less labour intensive than measurement by chemical means. The introduction of reference material (CRM 470) has standardised the transferrin assay and decreased the variance in reference ranges. High ferritin levels > 1000 ug/L were found to cause a positive bias in measured TIBC thus affecting transferrin saturation results, which could have clinical implications when screening for iron overload. Neither TIBC method appear to be affected by the level of albumin in serum.

Poster 11

Title: The Evaluation of the Total hCG Assay on the Immulite 2000™ Immunoassay Analyser

Authors: O'Kelly, R.A., O'Leary, J.J.

Address: Department of Biochemistry, Coombe Women's Hospital, Dublin 8, Ireland

Objective

To evaluate the analytical performance of the Total hCG assay on the recently installed Immulite 2000™ analyser (DPC). This assay is used to investigate early pregnancy (including ectopic pregnancy) and trophoblastic disease.

Methodology

This 30 minute assay for Total hCG is a solid-phase two-site chemi-luminescent immunometric assay and is linear between 1 and 5000 U/L with a 100-fold autodilution facility for higher results. Imprecision (intra- and inter-assay), functional sensitivity, carryover, linearity on dilution and bias were evaluated. Patient sera routinely requested for hCG analysis were combined into three pools: a low pool, close to the detection limit, a medium pool at the ectopic pregnancy decision limit, and a high pool, greater then the linear range of 5000 U/L, thus initiating the autodilution facility. A patient sample with a low but detectable hCG result was used to investigate the functional sensitivity. Commercial control materials were also analysed. Samples received from NEQAS were analysed to evaluate bias, using Analyse-It™ software.

Results

Intra-assay imprecision using 20 replicates of serum at two concentrations resulted in CVs of 6.3% and less. Inter-assay imprecision was evaluated using replicate measurements of the three pools over 20 days. The CVs obtained were 5.5% or less.

Functional sensitivity investigation showed a CV of 9.2% for a patient sample with hCG just above the detection limit. Linearity on dilution gave recoveries of 106% or less. No carryover was detected. The mean bias was 0.787 (95% C.I.-11.1 to +12.6)

Conclusion

This assay demonstrates good precision, linearity on dilution, no carryover and compares well with other users of this assay.

Poster 12

Title: Review of Porphyria in the Republic of Ireland

Authors: Crowley, V.E.F., Darby, C., O'Moore, R.

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

Introduction

The porphyrias are a heterogeneous group of genetic and acquired disorders of haem biosynthesis, which show protean clinical manifestations. For the optimal management of these disorders it is critical that the clinical, biochemical and genetic characteristics are defined for each specific population group.

Methodology

The Porphyrin Laboratory in St James's Hospital, Dublin, provides the only comprehensive porphyria diagnostic service for the Republic of Ireland (ROI). This service was established over 30 years ago, and has collated an array of biochemical and clinical information relating to both diagnosed probands and subsequent pedigree analyses. This archive forms the most extensive record available to date of the nature of porphyria within ROI.

Results

Since 1975 there have been 318 cases of biochemically confirmed porphyria of which 48% were related to sporadic porphyria cutanea tarda (sPCT). Acute intermittent porphyria was the most common acute porphyric disorder accounting for 19% of all cases.

Rather interestingly the prevalence of variegate porphyria (12%) and hereditary coproporphyria (9%) were very similar. The biochemical diagnosis of porphyria in Ireland has risen dramatically since 1990 and sPCT is the primary cause of this marked increase. Unsurprisingly, dermatology services are the most common source of referral of positive samples to our laboratory.

In acute porphyrias, females predominate as the initial probands presenting with acute neurovisceral episodes, which is consistent with findings in other populations. In 9 kindreds a genetic cause for the porphyria has been identified suggesting that porphyria in ROI is associated with a heterogeneous pattern of mutations.

Poster 13

Title: The Irish National Porphyria Database

Authors: Darby, C.,[1] Sullivan, G.,[2] Rennison, A.,[3] Marr, R.,[3] Brazil, N.,[1] O'Moore, R.R.,[1] Breen, E.,[1] Gannon, P.,[4] Crowley, V.E.F.[4]

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Department of Clinical Biochemistry, St. James's Hospital, Dublin 8, Ireland[4]

Introduction

At present the Biochemistry Department, St James's Hospital, Dublin is the only laboratory providing a comprehensive porphyria diagnostic service for the Republic of Ireland (ROI). The laboratory, with over 30 years of biochemical and clinical diagnostic experience, retains the most comprehensive record relating to the nature and extent of porphyria in ROI.

Outcome

Consequently, to coordinate this archive, a bespoke database was commissioned with very specific functional requirements. These included (1) a standard patient module with unique family identification (2) family tree generation facility (3) porphyrin result module (4) capability to integrate with the current hospital and laboratory information systems, thus allowing biochemical result and clinical data download (5) capability to interface with current analytical systems (6) word processing feature and (7) access to current acute porphyria safe drug list. Wren Computing developed a system based on these criteria.

Our database contains a full audit trail and is stored on a Microsoft SQL 2000 server with inbuilt FTP capability for data import. Analytical traces can be directly captured from laboratory screens and historical data can be scanned into the system. The family tree facility is highly visual in a rich windows environment.

Poster 14

Title: Development and Clinical Validation of a Method for Mutation Scanning of PPOX in Suspected Variegate Porphyria

Authors: Crowley, V.E.F., Collison, C., MacNamara, B., Balfe, A., Darby, C.

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

Introduction

Variegate porphyria (VP) is an autosomal-dominant disorder that is caused by inheritance of mutations protoporphyrinogen oxidase gene (PPOX) resulting in a deficiency of this enzyme in the heme biosynthetic pathway. VP is characterized clinically by cutaneous photosensitivity and/or acute neurovisceral episodes, and in many instances clinically overt VP is precipitated by exposure to specific environmental triggers e.g. drugs, menstrual cycle.

Overall, 70% of subjects with a pathogenic mutation in PPOX will not actually manifest with overt clinical disease throughout their lifetime, but it is difficult to predict who will fall into this category. Thus, all susceptible subjects who have not yet manifested overt VP are regarded as "presymptomatic" and should be provided with specific advice in relation to avoidance of environmental triggering factors.

Currently the biochemical tests used to detect latent or presymptomatic VP are of limited sensitivity (65-85%). Thus greater emphasis has been placed on the need to establish a molecular diagnosis of VP using PPOX mutation detection.

Outcome

In this report we describe the development and clinical validation of a sequencing-based method for PPOX mutation scanning. The clinical effectiveness of this system is demonstrated by the detection of a nonsense mutation (Q435X) in Exon 13 in a proband with clinically and biochemically diagnosed VP.

Moreover, this assay has been used to establish genotype-phenotype correlations within this VP pedigree.

Poster 15

Title: Lack of Association of P12A Polymorphism in PPARG with Type 2 Diabetes Mellitus in an Irish Population

Authors: Crowley, V.E.F., Denning, K., Stapleton, M., Balfe, A., Fitzgerald, A., Nolan, J.

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

Introduction

Type 2 Diabetes Mellitus (T2D) is now regarded as a serious public health epidemic associated with a high morbidity and mortality. In terms of aetiology it is widely acknowledged that T2D results from an adverse interaction between genetic and environmental factors. Thus, attempts have been made to determine susceptibility genes for T2D and recent studies suggest that P12A polymorphism in the gene for peroxisome proliferator activated receptor γ (PPARG) is associated with T2D predisposition.

Objective

The purpose of this study is to directly examine the association between P12A and T2D in an Irish case-control population.

Methodology

674 subjects were recruited to a case-control study for T2D in St James's Hospital, Dublin. RFLP-based methods were used for P12A genotyping on DNA extracted from the study population.

Results

Two RFLP-based genotyping assays were optimised and used to validate the genotype frequencies. The allele frequency for the minor allele (A) was not significantly different between T2D and normal glucose-tolerant (NGT) controls. In addition the genotype frequencies were in Hardy Weinberg equilibrium, but did not produce a significant difference between both groups studied.

Conclusion

Based on this study, the largest reported Irish T2D case-control study to date, the association between P12A and T2DM was not observed. This may reflect specific differences in the genetic makeup of the Irish population. We recommend that further replication of these findings be undertaken using a larger case-control group.

Poster 16

Title: Development and Validation of a Method for MC4R Mutation Scanning in Obesity

Authors: Crowley, V.E.F., MacNamara, B., Balfe, A., Yeo, G..

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

Introduction

Obesity is a disorder of chronic energy imbalance and is associated with serious morbidity and mortality. It is widely acknowledged that the prevalence of obesity has risen spectacularly over the last two decades and that it is now a major public health problem for both adults and children within most Western societies. In terms of aetiopathogenesis obesity results from an adverse interaction between genetic susceptibility and environmental risk factors.

Major insights into the molecular mechanisms underlying mammalian energy homeostasis, and consequently obesity, have been provided by the study of rodent and human monogenic obesity syndromes. While most monogenic forms of obesity are rare, it has become apparent that mutations in the gene for the melanocortin 4 receptor (MC4R), a nodal point in the leptin signalling pathway, are by far the commonest single gene cause of childhood-onset obesity.

In total over 40 different pathogenic mutations in MC4R have been associated with morbid obesity and it is estimated that 5% of severely obese children may have an MC4R mutation. This would strongly suggest that MC4R mutation scanning is a potentially important diagnostic test in the investigation of childhood-onset obesity.

Outcome

We describe the development of a method for mutation scanning of MC4R. Moreover, in collaboration with Professor Steve O'Rahilly's Laboratory, University of Cambridge, we have validated our assay system by detecting a series of MC4R mutations in patients from the Genetic of Obesity Study (GOOS).

It is now hoped to use this assay to determine the prevalence of pathogenic variants of MC4R in an Irish cohort with early-onset obesity.

Poster 17

Title: Evaluation of Immunoassay for Total Thyroxine on the AU3000i® Analyzer

Authors: O'Dea, P.G., Gaston, S., Brisson, C.

Address: Olympus Life and Material Science Europa GmbH.

Introduction

The Olympus T4 assay is a magnetic particle, chemiluminescent immunoassay for the quantitative determination of Thyroxine (T4) levels in human serum using the Olympus AU3000i®. Determination of Total T4 can be used for the diagnosis and confirmation of thyroid disorders: detection of hyperthyroidism, detection of primary and secondary hypothyroidism and monitoring of TSH-suppression therapy.

Methodology

We report here results from our development and evaluation of an automated assay for Total Thyroxine on the Olympus AU3000i® Analyzer. The assay is calibrated with nine gravimetrically prepared calibrators (0-240 µg/L).

Results

Lowest detectable level was determined to be 0.75 µg/L. Assay imprecision was characterized over 20 days (80 reps/instrument) according to NCCLS guidelines. Within run coefficient of variation (CV) for the Low, Medium, and High level human serum pools (20, 81, and 156 µg/L) ranged from 1.5 to 2.2%. Total inter-assay imprecision ranged from 2.7 to 4.5%. Specificity was determined by testing 9 analogues of T4 spiked into the zero calibrator. Cross-reactivity was ≤ 1% for 6 of the tested compounds. Cross reactivity levels of 85% were observed with D-T4 and Tetrac. 10% Cross reactivity was observed with Triac. The mean recovery of samples tested for linearity was 95.5%. No significant interference was detected from bilirubin, haemolysate, γ-Globulin, Intralipid, and HSA.

Conclusion

Based on our evaluation, we conclude that the AU3000i Total Thyroxine assay is a sensitive, precise, and accurate method for measuring Thyroxine levels in human serum.

Poster 18

Title: Evaluation of an Automated Immunoassay for the Determination of TSH (third Generation) on the Olympus AU3000i® Analyzer

Authors: Brisson, C., Fernandez, C., Minihan, M., Fitzgerald, D., Lentwojt, E.

Address: Olympus Life and Material Science Europa GmbH

Introduction

Olympus has developed an assay for the determination of TSH (Thyroid Stimulating Hormone) for our new automated immunoassay platform. Determination of TSH is used as an aid in the assessment of the thyroid status, diagnosis and treatment of thyroid disease. The Olympus TSH (third generation) assay is a para-magnetic particle, chemiluminescent immunoassay for the quantitative determination of TSH levels in human serum using the Olympus AU3000i® .

Methodology

We report here results from our development and evaluation of an automated assay for TSH on the Olympus AU3000i®Analyzer.

Results

Lowest detectable level was determined to be 0.0001µIU/ml. Functional sensitivity was 0.0056µIU/ml. Assay imprecision was characterized over 5 days (20 reps/instrument) according to NCCLS guidelines. Within run coefficient of variation (CV) for Low, Medium, and High human serum pools (0.0716, 1.44, and 28.2 µIU/ml) ranged from 1.7% to 4.7%. Between run coefficient of variation ranged from 4.2% to 7.1%. The AU3000i TSH assay is specific for TSH without cross-reactivity to LH, FSH, hCG. No significant interference was detected from bilirubin, haemolysate, Intralipid. Reagents were optimised to avoid RF and HAMAs interference.

Conclusion

Based on our evaluation, we conclude that the AU3000i® TSH third generation assay is a sensitive, precise, and accurate method which meets the requirements for measuring TSH levels in human serum especially by increasing the sensitivity.

Poster 19

Title: Evaluation of a New and Improved Olympus CRP Latex Assay on the Olympus AU400™, AU640™ and AU2700™ Analyzers

Authors: Larkin, T.,[1] McCusker M.,[1] Nicholas M.,[1] Hayes E.,[1] Gunzer G.,[1] Meek, J.[2]

Address: OlympusLife and Material Science Europa GmbH (Irish Branch) [1] Hammersmith Hospital, London, UK[2]

Introduction

CRP is one of the most sensitive acute-phase reactants providing information about acute and chronic inflammatory processes. CRP levels in serum can rise to almost 2000 times the normal (<1mg/L) after myocardial infarction, trauma, infection, inflammation or surgery. In contrast cord blood has very low CRP concentrations of approximately 0.12mg/L. The new CRP Latex assay OSR6199 has two applications which collectively span a range from 0.08-480mg/L. Olympus in conjunction with Hammersmith Hospital has evaluated this assay on the AU400, AU640 and AU2700 chemistry immunoanalyzers.

Outcome

This assay uses sample mixed with R1 accelerator buffer and R2 reagent containing latex material coated with anti-human CRP antiserum. Turbidimetric absorbance of complexes formed during the antigen-antibody reaction is measured at 570nm at 37ºC for approximately 5 minutes. The reaction is a calibrated fixed point method, utilizing 5 liquid stable multicalibrators traceable to CRM470/RPPHS. The Highly Sensitive application (HSA) has a lower detection limit of 0.07mg/l and is linear from 0.08-160mg/l. The Normal application (NA) has an upper measuring range of 480mg/l and is linear from 0.5-480mg/l. Prozone hook effect did not occur until >1000mg/L with the NA and >750mg/L with the HSA. Imprecision CV values are <5% for within run and <10% total CV for all analysers tested using NCCLS EP5-T2. Lipemic, haemolytic, icteric and rheumatoid interferences are <10% at levels (1000mg/L Intralipid, 5g/L haemoglobin, 684 µmol/L bilirubin, 560IU/mL RF) of each (NCCLS EP7-P). Reagent displays 30 day on board stability with recalibration necessary only every 30 days. The following table shows the excellent comparison of the assay on AU640 Dade Behring Nephlometry (BNII) and the current Olympus CRP Latex assay OSR6185.

Table 1: *Comparison of the Assay on AU640 Dade Behring Nephlometry (BNII) and the Current Olympus CRP Latex Assay OSR6185*

METHOD COMPARISON	BEHRING NEPHLOMETRY	BEHRING NEPHLOMETRY	OLYMPUS CURRENT ASSAY	OLYMPUS CURRENT ASSAY
Test method	New CRP assay NA	New CRP assay HSA	New CRP assay NA	New CRP assay HSA
Range (mg/L)	0.16-137	0.16-137	0.12-167.6	0.12-156.4
Slope	1.087	1.055	1.065	1.041
Intercept	0.319	- 0.230	0.812	0.325
Correlation coefficient	0.998	0.998	0.994	0.993
No. of samples	71	71	144	175

Poster 20

Title: Evaluation of Three Different Specimen Types (Serum, Plasma Lithium Heparin and Serum Gel Separator) for Analysis of Certain Analytes: Clinical Significance of Differences in Results and Efficiencies in Use

Authors: O'Keane, M.P., Cunningham, S.K.

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Introduction

There is a lack of consensus regarding the most appropriate specimen type for analysis of many biochemistry analytes. Identification of a single specimen type suitable for most analytes would result in significant savings and efficiencies.

Objective

The aims of this study were to determine if results for renal and lipid profiles and phenytoin are interchangeable in serum (plain and gel) and plasma lithium heparin blood collection tubes and to investigate the stability of these analytes in serum and plasma (1) after prolonged contact with cells or gel at room temperature (RT, 20ºC) and (2) aliquoted and stored at 4ºC.

Methodology

Primary specimens, plasma (P), serum (S) and gel (G), were simultaneously centrifuged once at 3000g for 10 minutes. Two aliquots from each tube were separated and stored at 4ºC for subsequent analysis at time 24 hours (T_{24}) and 48 hours (T_{48}). Triplicate samples (P, S & G) were analysed in duplicate for renal and lipid profiles and phenytoin at time 0 (T_0), T_{24} and T_{48}. Statistical significance ($p<0.05$) of differences from reference samples analysed at T_0 were determined by Friedman 1-way-ANOVA by rank, with the critical range test. Clinically significant differences were estimated as a function of imprecision and allowable bias.

Results

While minor but statistically significant differences were found for many of the analytes, when clinically significant differences were examined at T_0, all analytes in serum (plain and gel) and plasma were equivalent, except potassium, which showed a clinically significant increase in serum, plain (9.6%) and gel (7.1%), compared to plasma. All analytes, except $C0_2$ were stable when aliquoted, and stored at 4ºC. Phenytoin was stable in serum (plain) and plasma at RT but showed a clinically significant decrease in concentration at RT over time in serum gel.

Conclusion

Plasma was found to be the specimen of choice for the measurement of all the analytes investigated in this study. It was the most suitable for the analysis of potassium, provided that samples were analysed within two hours, otherwise, it was necessary to separate plasma from cells due to the instability of potassium over time. It was most favoured in terms of efficiency.

Poster 21

Title: Monitoring Changes in Biochemical Markers of Bone Turnover in Postmenopausal Osteoporotic Women Treated with Teriparatide

Authors: Healy, M.J.,[1] Cox, G.,[1] Casey, M.C,[2] Crowley, V.E.F.,[1] Coakley, D.,[2] Walsh, J.B.[2]

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Falls and Osteoporosis Unit, St. James's Hospital, Dublin 8, Ireland[2]

Introduction

Recombinant (1-34) Parathyroid Hormone (teriparatide) was approved for the treatment of osteoporosis in postmenopausal women in 2002. It is the first clinically useful bone forming agent that increases bone remodelling thereby promoting an increase in the production of bone formation and resorption markers. Biochemical markers of bone turnover can rapidly provide information on the early response to teriparatide therapy.

Objective

In this study we assessed the response of bone marker concentrations to teriparatide treatment in a group of postmenopausal women.

Methodology

Twelve postmenopausal women (mean age 75 years) who had severe osteoporosis and previous fracture were commenced on teriparatide (one 20µg subcutaneous injection per day). Bloods were taken at baseline and 3, 12, and 18 months post treatment. Samples were analysed for CTX (a bone resorption marker), Osteocalcin (OC) and P1NP (bone formation markers), and PTH. The assays were performed on an Elecsys 2010 immunoanalyser.

Results

In the first 3 months all bone markers increased significantly with formation markers increasing at a proportionally greater rate (OC:258% and P1NP:375%) than the resorption marker (CTX: 140%). Formation markers peaked at 12 months and declined thereafter. PTH levels decreased at 3 months and gradually increased at 12 and 18 months.

Conclusion

Monitoring bone markers give an early indication of the efficacy and compliance of teriparatide treatment. Net bone formation occurred for the first 12 months and this should be reflected in improved bone mineral density.

Poster 22

Title: Biological Day-to-Day Variability and Critical Differences in the Serial Measurement of Two Biochemical Markers of Bone Turnover in the Sera of Healthy Young Adult Males

Authors: Carroll, P.,[1] Jakeman, P.M.,[1] Barrett, E.,[2] Murphy, N.,[3] Donnelly, R.,[3] McLoughlin, M.,[3] and Murphy, M.[3]

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Clinical Biochemistry Department, Mid-Western Regional Hospital, Limerick, Ireland[2]
Human Behaviour Research Centre, Waterford Institute of Technology, Ireland[3]

Introduction

The purpose of this investigation was to quantify the biological day-to-day variability in serum levels of N-Mid Osteocalcin (OC; ng/ml) and CrossLaps (ng/ml) in healthy males (n=14). From this biological variation (CV_I: individual biological variability), the critical difference (CD) or least significant change was calculated. This value represents the minimal difference between two measurements of a biochemical marker that indicates a medically significant alteration of homeostasis (and is not due to normal biological and/or analytical variability alone). Given the CD of these markers the viability of using them in the assessment and/or monitoring of bone metabolism will be considered.

Methodology

14 males, 28±4 years with no known clinical disorder of bone or calcium metabolism participated in this study. All subjects were inactive, non-smokers and had not experienced a fracture or period of immobilisation in the six-month period prior to participation. Normal calcium intake was regulated by a prior 5 consecutive day dietary intake record (800mg/day) and alcohol consumption was not permitted for 3 days prior to and for the duration of the study. Blood (venepuncture, 8am-9am) samples were collected following an overnight fast (22h00) for 5 consecutive mornings. Serum was analysed for N-Mid Osteocalcin (OC; ng/ml) and CrossLaps (ng/ml) as measured by immunoassay (Roche Diagnostics, Elecsys 1010).

Results and Conclusions

1. Mean circulating levels of CrossLaps and N-Mid OC are 0.640 ± 0.265ng/ml and 32.72 ± 10.35ng/ml respectively, in this population.
2. The mean intra-individual CV_I for N-Mid OC is lower (~4%) than that for CrossLaps (~8%), which would indicate that N-Mid OC is a more stable marker. Inter-individual CV_I, however, as represented by the range of CV_I data is high for both markers.
3. The mean intra-individual CD is also lower (~12%) for N-Mid OC than that for CrossLaps (~22%), while again the inter-individual CD is in the region of 4 fold for N-Mid OC and 6 fold for CrossLaps.
4. The CV_I of serum CrossLaps is lower (~8%) than that previously reported for both urinary Pyr (21%) and dPyr (24%) in male and female subjects over 5 consecutive mornings. The estimated CD for Pyr and dPyr would therefore be 64.4% and 72% respectively. The impact of such biological variation on the viability of these markers of bone resorption in an acute setting has yet to be determined.

Poster 23

Title: The Components of Variance and the Critical Difference in Specific Markers of Bone Turnover in Healthy Adult Males and Postmenopausal Women

Authors: Carroll, P.,[1] Hunter, A.,[1] Barry, D.,[2] Barrett, E.,[3] Loughnane, M.,[4] Donnelly, R.,[4] Murphy, N.,[4] Jakeman, P.M.[1]

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Introduction

The purpose of this investigation was to quantify the components of variance in specific biochemical markers of bone turnover in healthy males and postmenopausal women i.e. total (CV_S), analytical (CV_A), within-subject biological (CV_I) and between-subject (CV_G) variances. Using CV_A and CV_I for each individual, the individual critical difference (CD_I) or least significant change ($P<0.05$) was calculated. This value represents the minimal difference between two measurements of a biochemical marker that indicates a medically significant alteration of homeostasis (and is not due to normal biological and/or analytical variability alone). Given the CD of these markers the viability of using them in the assessment and/or monitoring of bone metabolism will be considered.

Methodology

With ethical approval and informed consent, 17 healthy males (28.2 ± 1.0 years) and 13 healthy post-menopausal women (55.1 ± 1.2 years) who were not on HRT participated in this study. Subjects did not suffer from a known clinical disorder of bone or calcium metabolism. All subjects were inactive, non-smokers and had not experienced a fracture or period of immobilisation in the six-month period prior to participation. Normal calcium intake was regulated by a prior 5 consecutive day dietary intake record (800mg/day for males and 1200mg/day for females) and alcohol consumption was not permitted for 3 days prior to and for the duration of the study. Blood (venepuncture, 8am-9am) samples were collected following an overnight fast (22h00) for 5 consecutive mornings. Serum was analysed for N-MID Osteocalcin (OC; ng/ml) and CrossLaps (ng/ml) as measured by electrochemiluminescence (ECL; Roche Diagnostics). Following the first morning void (FMV) sample, 24h urine and a spot mid-flow FMV sample were collected for 5 consecutive mornings. All samples were analysed for total dPyr by ELISA and creatinine by HPLC.

Results

Table 1 Summary of the components of variance and critical difference for serum and urinary markers of bone formation and resorption in healthy males (n=17) and postmenopausal females (n=13). Data is represented as mean ± SD.

Biochemical Marker	CV_S (%)	CV_A (%)	CV_I (%)	CD_I (%)	CV_G (%)
Males (n=17)					
OC (mg/ml)	4.4 ± 1.6	1.6 ± 0.8	4.3 ± 1.7	9.5 ± 3.5	4.9
CrossLaps™ (ng/ml)	8.8 ± 3.8	2.2 ± 1.0	8.6 ± 3.8	19.0 ± 7.9	9.8
24h dPyr (nmol/d)	29.3 ± 10.9	6.0 ± 2.3	28.9 ± 11.1	63.0 ± 23.5	32.1
FMV dPyr (nmol/d)	33.9 ± 15.5	5.9 ± 2.6	33.6 ± 15.5	72.8 ± 33.3	39.7
Creatinine (nmol/L)	32.9 ± 19.9	1.2 ± 0.5	32.9 ± 19.9	70.7 ± 42.7	37.1
Females (n=13)					
OC (mg/ml)	5.7 ± 4.6	1.0 ± 0.4	5.6 ± 4.6	12.3 ± 9.8	7.1
CrossLaps™ (ng/ml)	9.4 ± 3.9	2.8 ± 1.7	9.2 ± 3.9	20.3 ± 8.3	3.1
24h dPyr (nmol/d)	23.0 ± 9.5	5.8 ± 2.4	22.6 ± 9.6	49.4 ± 20.5	26.6
FMV dPyr (nmol/d)	27.0 ± 8.3	5.4 ± 1.9	26.7 ± 8.3	57.9 ± 17.9	27.6
Creatinine (nmol/L)	27.9 ± 20.0	1.1 ± 0.7	27.9 ± 20.0	56.0 ± 42.8	36.5

Conclusions

The CD_I of a biochemical marker is an objective index of the ability of that marker to detect a change in bone turnover and given that biochemical markers of bone turnover are generally used in monitoring intervention strategies, it would appear that the marker with the best potential to detect change would be preferred.

1) As CV_A is common between subjects, CD_I is predominantly influenced by CV_I, which can vary greatly between subjects as evidenced by large SD values in Table 1.
2) With respect to the serum markers, the mean intra-individual CV_I for OC is lower (4.5% and 5.6%) than that for CrossLaps™ (8.6% and 9.2%) which would suggest that the marker of bone formation (OC) is a more stable marker for both groups. The corresponding mean intra-individual CD_I is also lower (9.5% and 12.3%) for OC than for CrossLaps™ (19.0% and 20.3%).
3) The mean intra-individual CV_I for the urinary measure of dPyr (marker of bone resorption) is 3.5 - 4 fold that of CrossLaps™ (serum marker of bone resorption) for the male subjects and 2.5-3 fold that of CrossLaps™ for the female subjects.
4) The mean intra-individual CV_I was for dPyr lower in the 24h (nmol/day) urine sample (28.9% and 22.6) than in the mid-flow FMV (nM/mM Cr) urine sample (33.6% and 26.7%) for both groups. The greater biological variation in the latter measure may be attributed to the need to correct this data for creatinine output which varies itself (37.3% and 27.9%). The corresponding mean intra individual CD_I is also lower for the 24h sample (63.0% and 49.4%) than for the FMV (72.8% and 57.9%) sample.

Poster 24

Title: Acute Effects of Anaerobic and Aerobic Exercise on Bone Turnover in Healthy Postmenopausal Women

Authors: Loughnane, M.,[1] Murphy, N.,[1] Donnelly, R.,[1] Barrett, E.,[2] Barry, D.,[3] Jakeman, P.M.,[4] Carroll, P.[1]

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Introduction

The human skeleton is a highly dynamic organ which resorbs and renews itself daily via a coupled process termed remodelling. Physical activity is a known prophylactic to many bone disorders and can perturb the remodelling process, either mechanically or metabolically. Using specific biochemical markers for bone resorption and renewal, this study sought to investigate the effects of two distinct acute (9 days) metabolic challenges on the bone remodelling cycle.

Methodology

With ethical approval and informed consent, 9 healthy, postmenopausal women, who were not on HRT were recruited (age; 55±1.1; height, 1.64±1.6; weight, 68.2±2.4; BMI, 25.5±1.1, mean ± SE). Following a 5 consecutive day baseline period, subjects completed an anaerobic (20mins at >AnT) and an aerobic (60mins < AnT) cycle ergometry exercise challenge. Each exercise period was 10-days in duration comprising 3-days of anaerobic or aerobic exercise followed by 7 days of recovery. A 10-day wash out phase separated the two exercise periods. Blood (venepuncture) samples were collected between 8am and 9am following an overnight fast (22h00) for each period of the study. Samples were analysed for N-MID osteocalcin, a marker of bone formation, and C-terminal fragment of pyridinium crosslinks (CrossLaps™), a marker of bone resorption, by electrochemiluminescence (Roche Diagnostics). The within-subject biological variation (CV_I) and individual critical difference (CD_I) for the baseline period were calculated for each subject according to Fraser and Harris (1989). Relative changes of post exercise data from the baseline mean concentration were normalised for CD_I and any deviation greater than ±2.15 (P=0.05) was considered to reflect a significant perturbation in cellular function.

Results

The mean concentration of serum osteocalcin and CrossLaps™ was 32.98±7.74 ng/ml and 0.65±0.18ng/ml respectively. The group mean CV_I (6% v 9%) and CD (14% v 19%) were lower for the bone formation marker. However, the between subject variance in CV_I was large for both markers (OC; 0.9-15.6%, CrossLaps™; 2.7-17.5%) and this is reflected in the degree of imprecision, h (=$1/2\beta$), between the observed mean and true biological homeostasis. The nature of the variance of OC changed in the majority of subjects following both exercise interventions. Grouping the daily responses to the anaerobic challenge 37% of the data deviated beyond the limits set at ±2.15, (25% in a positive direction). The anaerobic challenge had little effect on osteoclast activity as measured by serum CrossLaps™. A biologically significant change was only seen in 17% of the data, 15% in a negative direction. The net effect of this exercise challenge was not significant for any subject. 23% of the data was significantly perturbed in response to the aerobic exercise challenge (1% in a positive direction).

Conclusions

Bone remodelling, as measured by specific biochemical markers, was significantly perturbed following discrete bouts of anaerobic and aerobic exercise. By grouping the data, it would appear that the net effect of the anaerobic trial was an uncoupling of remodelling in favour of formation while the net effect of the aerobic trial was an overall reduction in the rate of remodelling. However, at an individual level the nature of the perturbation differed between subjects with respect to the magnitude, the timing and the direction of the perturbation. We believe that due to the complex nature of skeletal tissue remodelling the physiological impact of the perturbation observed on BMD cannot be resolved in such an acute setting. The use of biochemical markers in an acute setting can only be possible once the relationship between changes in biochemical markers and BMD have been established.

Poster 25

Title: Cost And Appropriate Use Of Laboratory Testing: An Assessment Of Doctors' Knowledge

Authors: Kearney, D.,[1] O'Leary, P.,[1] Stapleton, M.,[2] O' Mullane, J.[2]

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Objectives

To determine doctors' awareness of the costs of commonly ordered blood tests. The study also aimed to ascertain if doctors order unnecessary tests, along with whether they recognise changing trends in laboratory results that are within normal parameters.

Methodology

The study was conducted in the Mercy University Hospital (MUH), Cork, a 354 bed acute general hospital in Cork city centre. The study population was 68 non-consultant hospital doctors and the response rate was 69%. The questionnaire consisted of ten questions in multiple choice answer format. Questions included doctors' opinion about the number of laboratory tests being ordered in the hospital; the cost of commonly ordered blood tests; the appropriate interval between repeat tests; the best time to check plasma paracetamol levels in overdose; and recognising changing trends in laboratory results that were within normal parameters.

Results

- 84% of doctors believe that too many laboratory tests are performed in the hospital.
- Overall, doctors overestimate the costs of the inexpensive tests and underestimate the costs of the expensive tests.
- The majority of doctors know when to repeat paracetamol levels in an overdose.
- 49% of doctors know the correct interval to repeat common laboratory tests.
- Doctors have significant difficulty recognising changing trends in laboratory results that were within normal parameters.

Conclusion

This study highlights doctors' dissatisfaction with the volume of laboratory tests being undertaken in the MUH, along with their general lack of awareness about the cost and appropriateness of these tests. This important issue needs to be addressed in current practice and further study needs to be undertaken in this area.

Poster 26

Title: Comparison of Selected Physicochemical Characteristics of Lactases from over the Counter Lactase Digestive Supplements Relevant to their Application in the Alleviation of Lactose Intolerance

Authors: O'Connell, S.

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Introduction

Microbial derived lactases are administered as digestive supplements for the hydrolysis of dietary lactose in lactase deficient individuals.

Methodology

A series of *in-vitro* experiments were carried out to determine the relative suitability of four lactase digestive supplement products for use in alleviating the symptoms of lactose intolerance.

Results

The enzymes assessed lost all of their original activities after incubation in simulated gastric fluid for 1 min when extracted from their tablet/capsule formulations. After exposure to simulated intestinal conditions for 4 h, the lactases assessed retained between 85 and 97% of their original activities. The tablet/capsule formulation of the supplements was found to be critical for maintaining the lactase activity when exposed to simulated gastric fluid. The Lifeplan lactase digestive supplement capsules were found to be the most effective in hydrolysing lactose when exposed to simulated gastro-intestinal conditions *in vitro*. However the capsules only hydrolysed 22% of the lactose load. The lactases displayed between 55-61% of their maximum activities at 37ºC and displayed optimum activity between pH 3.5 and pH 5.5. The enzymes displayed K_m values for lactose ranging from 110-260mM.

Conclusion

None of the lactases assessed satisfied all of the criteria of an ideal lactase for use in the alleviation of lactose intolerance.

Poster 27

Title: Development of Optimised Small Volume Sample Settings 'Paediatric Settings' for 22 Parameters on the Olympus AU400™/AU640™, AU600™ and AU2700™ Analysers

Authors: Larkin, T., O'Connor, N., Hayes, E., Kretzschmar, F., Gunzer, G.

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Introduction

In infants less than one year old, the volume of sample that can be collected is typically very small. This often limits the number of assays that can be carried out with such a sample. Olympus has developed optimised small volume serum sample settings, termed 'Paediatric Settings' for use with the following Olympus analysers: AU400/640, AU600 and AU2700/5400.

Objective

The purpose of the 'paediatric settings' is to conserve sample volume for any small volume patient sample.

Methodology

The use of a 10 µl sample diluent will eliminate the 5 µl sample volume wastage with each dispensing step. This will save 5 µl of precious sample volume for small volume samples. These settings are available for 22 of the Olympus System Reagents (Albumin OSR6x02, ALP OSR6x03, ALP OSR6x04, ALT OSR6x07, AST OSR6x09, D-Bilirubin OSR6x11, T-Bilirubin OSR6x12, Calcium oCPC OSR6x13, GGT OSR6x20, Glucose OSR6x21, LDH OSR6x26, LDH OSR 6x28, Triglyceride OSR6x33, Urea OSR6x34, IgM OSR6x46, Transferrin OSR6x52, C3 OSR6x59, C4 OSR6x60, Calcium-Arsenazo OSR6x76, Creatinine OSR6x78, Iron OSR6x86 and Bicarbonate OSR6x90).

For all parameters, within-run precision and control recoveries are within specification and comparable to results achieved using normal settings.

Results

Results of method comparisons for 5 representative parameters showed good correlation between paediatric and normal settings: Glucose OSR6x21 (low sample volume assay) Y=0.997x - 0.189, (r)=0.999; Calcium Arsenazo OSR6x76 (end-point assay) Y=1.034x - 0.061, (r)=0.999; C3 OSR6x59 (immunoassay) Y=0.964x - 0.022, (r)=0.996; Iron OSR6x86 (high sample volume assay) Y=0.997x + 0.407, (r)=1.000 and GGT OSR6x20 (enzyme assay) Y=0.971x + 0.771, (r)=1.000.

In addition to the introduction of a 10 µl sample diluent to minimise wastage, the primary wavelength was changed from 540 to 570 nm for the T-Bilirubin assay OSR6x12.

This change will significantly reduce haemolytic interference from 50% to ≤20% up to 5g/l haemoglobin, which is critical for paediatric samples. The sensitivity however is lower at 570 nm, which results in slightly reduced precision at the low end (concentration 0.43 mg/dl results in normal CV=0.9%; Paediatric CV=1.6%), for this assay only.

Conclusion

Typically 'Paediatric settings' may be used by laboratories on Olympus analysers as a separate panel of tests for use with small volume samples only, or they may be used instead of 'normal settings' for any normal and small volume sample analysis.

Poster 28

Title: Performance Evaluation of an Automated Immunoassay for the Determination of LH (Luteinizing Hormone) on the Olympus AU3000i® Analyzer

Authors: Brisson, C., Kelly, H., Flanagan, P., Lentwojt, E.

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Introduction

Olympus has developed an assay for the determination of LH for the new automated immunoassay platform. Determination of LH is useful for the diagnosis and confirmation of hypothamamic-pituitary-gonadal disorders and can be used for the treatment of infertility in women and prediction of ovulation.

The Olympus LH assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of LH levels in human serum using the Olympus AU3000i®.

Methodology

We report here results from our development and evaluation of an automated assay for LH on the Olympus AU3000i® Analyzer.

Results

Lowest detectable level was determined to be 0.04 mIU/ml. Assay imprecision was characterized over 20 days (80 reps/instrument) according to NCCLS guidelines. Within-run coefficient of variation (CV) for Low, Medium, and High human serum pools (6, 30, and 90 mIU/ml) ranged from 1.7to 1.93%. Between-run coefficient of variation ranged from 4.6 to 5.4%. No significant cross-reactivity was detected from FSH, TSH, hCG, hGH. The mean recovery for samples tested for linearity was from 93% to 108%. No significant interference was detected from bilirubin, haemolysate or Intralipid. Reagents were optimised to avoid RF and HAMAs interference.

Conclusion

Based on our evaluation, we conclude that the AU3000i® LH assay is a sensitive, precise, and accurate method for measuring LH levels in human serum.

Poster 29

Title: The Biomedical Application of Atomic Force Microscopy to a Point-Of-Care Measuring System for a Model Test Antigen

Authors: Sheehan, A.[1]; O'Mullane, J.[1]; O'Connell, B.[2]; Crowley, M.[1]

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Introduction

The BioFinger, a point-of-care measuring system, will be a diagnostic tool based on the measurement of molecular (antibody-antigen) interactions by integrated micro- and nano-cantilevers using Atomic Force Microscopy (AFM) technology.

Objective

The role of Cork University Hospital in this project is to develop a surface chemistry for the immobilisation of biomolecules onto the cantilevers, allowing for compatibility with fabrication processes.

Methodology

Prostate specific antigen (PSA) was chosen as a model test antigen. Epitope mapping allowed for specific monoclonal antibodies for both free and total-PSA to be purchased and ELISAs for both to be developed, optimised and validated on polystyrene microtitre plates. Gold-coated silicon wafers (4mm x 4mm) were used as larger models of the cantilevers and an immobilisation technique was developed.

Results

This novel immobilisation technique was completely optimised and validated.

Conclusion

AFM imaging has allowed for physical proof of the developed immobilisation technique, using a method which integrates the attachment of goat-anti-mouse antibodies conjugated to 15nm diameter colloidal gold to the primary immobilised antibodies.