

Clinical Biochemistry News



ACBI



ACB

October 2013

Newsletter of the Association of Clinical Biochemists in Ireland
and the Association of Clinical Biochemists (Republic of Ireland Region)



**The Club Wall at the GAA Museum, Croke Park
Contains plaques of every GAA club both inside and outside Ireland**

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Contents

- | | |
|---|--------------------------|
| 2. From the President | 6. New Technologies |
| 3. Around the Web / Members' Publications | 7. Croke Park / Meetings |
| 4. Reports from Focus 2013 | 8. Nobel Prize Time |
| 5. In the Literature | |

Newsletter will be posted on the ACBI website where hyperlinks will be available

From the President

Ruth O’Kelly

As President of the Association of Clinical Biochemists in Ireland, I would like to welcome you to the 2013 Conference edition of our association’s newsletter. This year’s annual conference is being held again in the Croke Park Stadium and promises to be as good if not better than our very successful conference last year. This has been a great choice of venue and anyone I spoke to during the year particularly mentioned how impressed they had been.

Last year, the conference celebrated the fact that Dublin was declared City of Science 2012. This year the conference organising committee have taken the 2013 year of the Gathering – a year-long celebration of everything Irish -as their theme. The Gathering has been an important cultural event in Ireland this year. People all over the world have been encouraged to come to Ireland and it is events such as this which gives people a focus around which to plan their visit. I don’t know if anyone reading this has chosen to visit Ireland and come to our conference as part of this Gathering celebration, but if you have you are very welcome.

Statutory registration is fast approaching and an important component of this will be CPD for which such meetings provide a pleasant means of achieving our requirements. Coru has been set up to regulate the health and social care professions and thus protect patients. More information can be found on our website (www.acbi.ie) or on the Coru website (www.coru.ie).

Clinical biochemists have been to the fore of many developments and innovations in laboratory medicine in Ireland. The annual ACBI conference and other meetings hosted throughout the year showcase the developments and professional enthusiasm of the ACBI members. Many clinical biochemists are fellows of the Royal College of Pathologists (RCPATH, UK) and many others lead specialist services. The profession faces many challenges today, not least is our decreasing numbers due largely to the moratorium in recruitment, meaning that we need to punch above our weight in scientific and clinical developments. To this end, a partnership is underway between the Clinical Biochemists in Ireland, the Royal College of Pathologists (UK), and the Royal College of Surgeons to advance an Institute of Clinical Science, which will have the potential to lead developments in the clinical sciences in diagnostic laboratory and, in time, other areas of medicine.

Many scientific innovations are lost in translation between academic centres and diagnostic laboratories. The Institute, combining the assets of an innovative academic college in RCSI, together with specialist postgraduate training and diagnostic service planning expertise of RCPATH will facilitate clinical scientists to have critical mass in terms of profile, career definition and opportunities in collaborative research.

With support and investment of the participating colleges and scientists, the outcomes of the Institute will translate into access to optimal scientific and diagnostic advances for Irish patients.

There is a wide and varied list of topics at our conference this year, all relevant to the practice of Clinical Biochemistry in Ireland today. The first day’s topics include Cancer, Bone and Brain with presentations on molecular diagnostics in oncology, the war on cancer, osteoporosis, dementia, brain injury and treatment of epilepsy. Saturday’s programme will focus on the clinical use of diagnostic tests followed by three presentations on creatinine standardisation and kidney disease.

Our conference is an opportunity to renew friendships, make new contacts and socialise with other laboratory professionals and corporate colleagues. This aspect, in some ways, is as important as the scientific content. I welcome all our colleagues from other disciplines and professions to our conference. A special thank-you to our colleagues in industry for their financial support both this year and in previous years. Such meetings could not take place without your involvement .

I know you will enjoy this 36th annual conference of the Association of Clinical Biochemists in Ireland which has been organised by Ger Collier and her team at Beaumont Hospital and once again I look forward to meeting you all in Croke Park.

Ruth O’Kelly
President Association of Clinical Biochemists in Ireland.

Around the Web

@ChemistryWorld

Twitter account of the Chemistry Magazine published by the Royal Society of Chemistry. Links to some interesting articles.

Clinical Chemistry Learning Resources

From Cardiff University (Duncan Cole) a useful set of tutorials on bread and butter stuff.

Interpreting Changes in Troponin—Clinical Judgment Is Essential

From Clinical Chemistry: A Case Study

Take with a Grain of Salt

Interesting neonatal case study from Clinical Chemistry

Ernest Walton

The Nobel Prizes are being presented this week (first 2 weeks in October). As it happens October 6th 2013 is the 110th anniversary of the birth of Ernest Walton. He is Ireland's only winner of the Physics award (1951) and, in fact, our only science-based awardee.

Fructose: It's "Alcohol Without the Buzz"

Robert Lustig (Professor of Clinical Pediatrics, University of California San Francisco) has, over the last number of years, been warning about the dangers of fructose overconsumption and its links with the worldwide obesity epidemic. The above article comprehensively reviews fructose metabolism and biochemistry and its putative role in obesity, metabolic syndrome and hepatic insulin resistance.

Ortho Clinical Diagnostics, manufacturer of the Vitros range of chemistry analysers and IVD tests has been put up for sale by its parent company Johnson and Johnson. It has been estimated to be worth up to \$5 billion.

Members' Publications

Brady JJ, Crowley RK, **Murray BF**, **Kilbane MT**, **O'Keane M**, McKenna MJ. Limited utility of tartrate-resistant acid phosphatase isoform 5b in assessing response to therapy in osteoporosis. *Ir J Med Sci*. 2013 Jun 5. [Epub ahead of print]

McBrierty D, Wilkinson A, Tormey W. Drug-facilitated sexual assault evidence: an Irish perspective. *J Forensic Leg Med*. 2013 May;20(4):189-97.

O'Sullivan EP, Duignan J, **O'Shea P**, **Griffin D**, Dinneen SF. Evaluating hyperglycaemia in the hospitalised patient: towards an improved system for classification and treatment. *Ir J Med Sci*. 2013 Jul 2. [Epub ahead of print]

O'Sullivan EP, Ashley DT, Davenport C, Penugonda L, Kelleher G, Devlin N, Crowley R, **O'Shea P**, Agha A, Thompson CJ, O'Gorman DJ, Smith D. A comparison of osteoprotegerin with adiponectin and high-sensitivity C-reactive protein (hsCRP) as a marker for insulin resistance. *Metabolism*. 2013 Jan;62(1):34-8. : Epub 2012 Jul 27.

O'Shea P, O'Connor C, Owens L, Carmody L, Avalos G, Nestor L, Lydon K, Dunne FP. Trimester-specific reference intervals for IFCC standardised haemoglobin A(1c): new criterion to diagnose gestational diabetes mellitus (GDM)? *Ir Med J*. 2012 May;105(5 Suppl):29-31.

O'Sullivan ES, van der Kamp S, **Kilbane M**, McKenna M. Osteogenesis imperfect in adults: phenotypic characteristics and response to treatment in an Irish cohort. *Ir J Med Sci*. 2013 Aug 6. [Epub ahead of print]

Walsh JM, McGowan CA, **Kilbane M**, McKenna MJ, McAuliffe FM. The relationship between maternal and fetal vitamin D, insulin resistance, and fetal growth. *Reprod Sci*. 2013 May;20(5):536-41.

Two Reports From Focus 2013, York, 14th - 18th April

Orla Maguire, St. Vincent's University Hospital, Dublin

This year Focus tried out a new format in an effort to cut costs. It was held in the Exhibition Centre, York University - a venue that was considerably smaller than the Convention Centres used in the past. Accommodation was available on campus in the student rooms. The facilities at the Exhibition Centre were very suitable with possibly more space required for posters.

Report from Tuesday 16th April 2013.

Current Questions in Endocrinology Session:

Dr Carol Evans from Cardiff opened this session with a comprehensive review of the impact of method differences on the interpretation of cortisol measurements. She presented data that showed significant differences of results between methods and in addition method differences between male and female samples. Such are the differences that method dependent cut offs for the Synacthen test and the possibility of separate reference ranges for women on the pill may need to be considered. Prof Andy Levy then gave a very entertaining presentation on how cortisol excess can be diagnosed. He always ask his patients to bring an old photograph of themselves to distinguish between an intrinsic obesity issue or progressive features of hypercortisolaemia! The best tests to use include salivary cortisols (which may in time, once more evidence is gathered, be the test of choice), 24 hour urinary free cortisols and dexamethasone – suppressed CRH test.

Back to Basics Session:

Dr Salman Razvi from Tyne and Wear gave a presentation on Thyroid Function Tests. He emphasised the diurnal rhythm of TSH; highest

levels are seen between 9am – 12 mid day and lowest levels between 4 and 6pm. He also emphasised the effect of ageing on TSH levels suggesting that the upper level of the reference range should rise to 5.9 mIU/L between the age of 70 and 79 and increase to 7.5 mIU/L after the age of 80. Plasma free T4 also increases after the age of 60. This was followed by a presentation from Dr Steve Ball from Newcastle who is part of a European wide collaboration in the process of publishing guidelines in the diagnosis and treatment of hyponatraemia. These guidelines are due to be published in late 2013 and we were given a sneak preview. This will have implications for laboratory practice as serum/ urine osmolality and urinary sodium have moved up the top of the algorithm replacing the concept of first deciding the volume status of the patient. Dr Stephen Ryder from Nottingham gave a presentation on Liver Function tests. He outlined how current liver test panels are deficient in including a marker of fibrosis. Markers of fibrosis include Hyaluronic acid, ELF and Fibrotest and studies have shown that these tests predict liver related outcome over time better than liver biopsy. Raised ALT levels can be non specific in many primary care patients with no diagnosis reached in half of these patients. Indeed, a raised ALT may be more predictive of cardiac death than it is of liver disease since fatty liver, part of the metabolic syndrome (associated with cardiovascular risk) is a common cause of a raised ALT.

Mary Stapleton, Coombe Hospital, Dublin

In April 2013 I was fortunate enough to obtain funding through the ACBI to attend the Focus conference in York. The theme of the conference was 'Back to Basics', and the breadth of subjects allowed for a wide range of up-to-date topics to be

discussed. Subjects covered ranged from demand management and retesting intervals to arguments relating to the fitness for purpose of commonly used analytical profiles such as liver function tests.

A well-attended lunchtime debate on the usefulness and benefit of point of care analysers outside the laboratory brought up quite a number of interesting points, though the well researched arguments of the debator did little to alter the original opinions of the majority of the audience.

The plenary lectures varied from research-based talks requiring a large amount of concentration to a gentle stroll through the career of William Marshall to a synopsis of budgeting in laboratory medicine.

One lecture of note was on the topic of laboratory amalgamation and reconfiguration. Given by Ruth Lapworth it was extremely interesting and relevant, when one considers the Hospital Groups proposals currently under way within the HSE. Starting from an outline of the unique geography and location of hospitals within the region, we were shown changes in structure and operating schedules in the region. Starting with the establishment of a Quality Management Framework, the remodel of the group used a variety of methods to improve efficiency by initially implementing integrated information technology. The change across all departments has been considerable. There was extremely poor morale with a loss of identity and a 'silo' mentality at the beginning. Since completion of the reconfiguration, however, and although working hours have changed considerably with a 7 day working week, there is increased interest and pride within the laboratory. This has also been brought about by introducing journal clubs, allowing for further education qualifications with the aim of bringing more staff to state registration, as well as receiving recognition of the work done by way of a health business award for the advances within the laboratory.

The number and variety of lectures, posters and social events kept me busy over the course of the conference, and I hope to have brought at least some fresh ideas for use in the course of my own working day.

In the Literature

People generally take randomised controlled trials (RCTs) as gospel. If RCTs conclude that something is good bad or indifferent then it must be so. Many guidelines are produced based on the findings of RCTs the assumption being that RCTs are the gold standard of evidence. The conclusions of RCTs founded on the evidence-base are often accepted without question. There are some dissenting voices however. A paper recently published in the *Mayo Clinic Proceedings* (Prasad V, Vandross A, Toomey C, et al. *A decade of reversal: an analysis of 146 contradicted medical practices*. *Mayo Clin Proc*. 2013;88(8):790-8) points out that of the RCTs published in the New England Journal of Medicine (NEJM) over the past 10 years 46% have been subsequently reversed. An accompanying hard hitting editorial (by JPA Ioannadis) calls this a 'disastrous' state of affairs. The editorial can be found [here](#). He leaves us in no doubt about the implications of poorly designed low quality RCTs and the possible impact they are having on scarce medical resources not to mention public health. The NEJM was chosen for this investigation because it is the most widely read of the general medical journals with the highest impact factor. It is read by policy makers worldwide and is used by many in the formulation of guidelines.

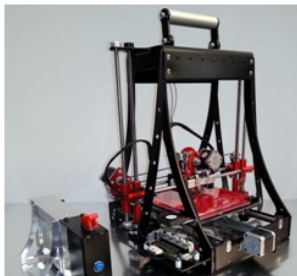
Ioannadis has been publishing on this issue for a number of years. In a 2005 paper in *PLOS Medicine* (*Why most published research findings are false* -read it [here](#) and read a review of the paper [here](#)) Ioannadis uses mathematical modelling to show that most claimed research findings are false and simply flipping a coin may be as useful as a clinical finding in support of a hypothesis. Using the concept of positive predictive value (PPV), i.e. a positive finding is a true finding he outlines several ways the PPV may be influenced in a study. An interesting one is the paradoxical relationship between the number of independent investigators on a topic and the PPV for a given study in that field—the hotter the field, the more spurious the science.

New Technologies

Gradually the futuristic technologies seen on Star Trek are coming to pass. Recently a prize was offered to manufacture a tricorder which would monitor a series of vital signs and deliver a digital readout of the results. To win the prize (\$10m sponsored by Qualcomm), the device must be light weight and “capable of capturing key health metrics and diagnosing a set of 15 diseases”. The original tricorder, used by Dr. Leonard McCoy (‘Bones’) on the USS Enterprise, was able to diagnose any disease just by scanning different parts of the body. Such a device is a long way away but already several companies have joined the race for the prize. At this early stage a device has been developed by Scanadu, a Silicon Valley based company. Known as the Scout™ it is a small hand-held sensor which, when pressed against the forehead, tracks temperature, respiratory rate, systolic and diastolic blood pressure, blood oxygenation, pulse transit time and stress level. It operates with a companion app and is in the final stages of development.



Scanadu Scout™



Example of a 3D Printer



A Bioprinted Ear

Another new technology which has come to the fore recently is the 3D printer. It is a primitive ancestor of Star Trek’s replicator which Captain Jean Luc Picard of the Starship Enterprise used to order “tea, earl grey, hot”. While we are not at the stage of voice-operated replicators 3D printers can do some amazing things.

The first 3-D printer was invented by Chuck Hull in 1984. He called the process stereolithography (the term “3D printer” came later). The basis of 3D printing is quite different from the traditional manufacturing process which uses what is called subtractive manufacturing. This is essentially breaking down an object (a block of wood for example) to produce another one (a coffee table say) by means of cutting, sawing, planing, hammering etc. 3D printing uses an additive process i.e. it is the creation of a three dimensional object by building layer upon layer from the bottom up with little waste. The process is controlled by CAD type software. The technology was quickly picked up by industry but the hardware was very bulky and very expensive. In more recent years several different types of additive printing have been developed and ‘personal’ 3D printers have emerged. What can be ‘printed’ by them? The answer is anything for which a 3D image can be generated and is a size the printer can handle. This can include jewellery, toys, machine parts, the components of a 3D printer etc.

More recently the technology has been used to print biological material. The procedure is known as bioprinting and is defined as “the construction of a biological structure by computer-aided, automatic, layer-by-layer deposition, transfer, and patterning of small amounts of biological material”. Jawbones, ears and noses have been printed using this process. These structures are inert, however, and lack a vascular system. Significant research is being done on how to print vascularised material. An advantage of tissue printing lies in the fact that individual items can be printed according to a patient’s needs. The ultimate aim is to print entire organs from a patient’s own tissue. At a stroke this would do away with transplant waiting lists. This is probably decades away, though, and must overcome the issue of vascularisation mentioned above.

Are there disadvantages? Yes. Printing can take from several hours to a day per item. The hardware is still expensive. They only print in one type of material at a time whereas manufactured goods can contain several. Items printed may not be as robust as their manufactured counterparts. Many of these drawbacks will be overcome in time.

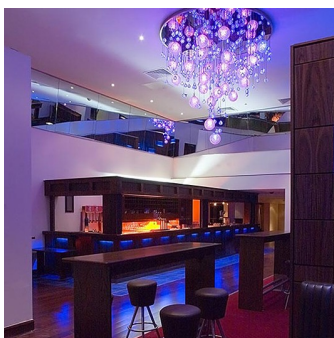
Croke Park – Venue for ACBI 36

We're back in Croke Park this year for the Annual Conference. The stadium is the 4th biggest in Europe and it can hold over 82,000 spectators. In excess of 2 million patrons pass through its turnstiles each year. The Croke Park site has been associated with sport since 1884 and it gained stadium status in 1913. As a corporate entity the stadium hosts close on 100 events a year (this one included) and has become a major player on the conference circuit. In May 2010 it received BS 8901 certification for sustainable event management, the first stadium in the world to do so. This standard, aimed at the events industry, defines requirements for a balanced approach to economic activity, environmental responsibility and social progress relating to events. Also, in 2009 the stadium was awarded ISO 14001:2004, a standard associated with environmental management systems.

Croke Park doesn't do things by half-measure. It has the biggest outdoor screen in Europe situated at the Hill 16 end. The Davin Bar has over 400 taps making it the largest bar in Ireland, maybe even in Europe. There are 3 km of seating and 463 floodlights. The Park attracts important visiting dignitaries. Queen Elizabeth II and the Duke of Edinburgh visited in 2011 and in 2012 Xi Jinping, then Vice-President now President, of China was welcomed. While there he practiced his Gaelic skills by kicking a ball and hitting a sliotar.

One of the highlights of the stadium is the players' lounge where the Annual Dinner for ACBI 2013 will take place. The centrepiece of the lounge is the Waterford Crystal chandelier. Designed by Billy Canning it consists of 32 crystal Gaelic footballs representing the 32 counties and 70 sliotars representing each minute of a game in a full championship match. The crystal can be adapted to a winning team's colours using LED technology.

All in all an impressive venue and one the country can be proud of.



Players' Lounge and Chandelier



**Outdoor Screen
(with the words of Ireland's Call)**

Meetings

BSG 2014 Manchester Central Convention Complex, UK - 16th-19th June 2014
(Annual Meeting of the British Society of Gastroenterology)
www.bsg2014.org.uk

Lipid Update XII London UK 25th November 2013
www.lipid-update.com

Society for Endocrinology BES 2014. 24-27 March 2014 - The ACC Liverpool UK
www.endocrinology.org/meetings/2014/sfebes2014/

NGS 2013 MANCHESTER, UK "Applications & Bottlenecks" (Next Generation Sequencing). Manchester Conference Centre, 5th - 6th November 2013
www.conference.biotexcel.com/ngs-2013 manchester/

Epigenomics of Common Diseases. 7-10 November 2013 Wellcome Trust Conference Centre, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK
[https:// registration.hinxton.wellcome.ac.uk/display_info.asp?id=356](https://registration.hinxton.wellcome.ac.uk/display_info.asp?id=356)



Nobel Prize in Physiology or Medicine - 2013

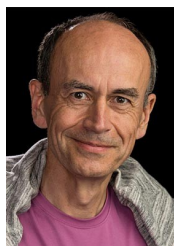
Many of you, in your undergrad years, will have seen drawings or electron micrographs of intracellular vesicles in various textbooks and may not have given them much thought. They are in fact vital to normal intracellular function and this year's Nobel Prize for Physiology or Medicine recognises this. The 2013 Prize has gone to two Americans, James Rothman (Yale University) and Randy Schekman (University of California at Berkeley) and German-born Thomas Südhof (Stanford University) *"for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells"*. The citation underplays the complex life-cycle of these little organelles. Vesicles are bubble-like membranous sacs that transport cellular products and digest waste. They are separated from the cytosol by at least one lipid bilayer and allow movement of molecular components from one area of the cell to another or facilitate extrusion into the extracellular milieu. The pathways involved in this process were elucidated by the laureates. Randy Schekman discovered the genes that are required for intracellular vesicle transport. James Rothman discovered the mechanism whereby vesicles fuse with membranes to release their cargo and Thomas Südhof revealed how signals instruct vesicles to release their contents when required. Breakdown in any of these steps leads to disease, with increasing evidence of vesicle malfunction in diabetes and immune disorders. Biographies, some details of their work and links can be found [here](#).



**James E.
Rothman**



**Randy W.
Schekman**



**Thomas C.
Südhof**

The awards confirm the grip the US has on the Nobels. Remarkably, they have won at least one of the 6 categories every year since 1936. They won their first award for physiology or medicine in 1933 and, according to the Nobel Prize web page, have gone on to win it 69 times. The nearest rival in the winning stakes for this category is the UK with 23 successes. The gender balance is decidedly skewed towards males with no female winners of the medicine prize coming from the UK and just 5 from the US. In fact, out of all Nobel Prizes awarded since their inception just 5% are female laureates.

There is no correlation between population and number of Nobel Prizes won. The US, with a population of 314 million have a total of 251. China with a population of 1.35 billion have 10. India with a population of 1.24 billion have 6. Similar small numbers can be seen for other densely populated countries.

Interestingly, comparing the number of prizes won per head of population since 1901, the first year the prizes were awarded, the US (1:1.3M) does not come out on top. This honour falls to the UK (1:808K). However, over time the gap between the US and the UK has been widening. For the first 40 years of the prizes it was even between the two countries (22 for the UK, 23 for the US). Over the next 40 years the gap between the countries widened considerably (36 for the UK and 100 for the US). In the last 30 years UK figures have contracted somewhat and US figures continue to rise (20 for the UK and 128 for the US). Nevertheless, the UK still has the largest haul of prizes in Europe followed by Germany. [All stats are from [nobelprize.org](#)]

A clue to US superiority could be that they have 20 universities in the world's top 50. These include this year's winners (Yale 7th, Stanford 15th and UC Berkeley 22nd). The UK has 8, the second highest number. Both of these countries have little problem attracting the highest calibre academics.