
Clinical Biochemistry News



ACBI



ACB

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



Reception in Áras an Uachtaráin

President Mary McAleese and Dr Martin McAleese invited Dr Philip Mayne, Dr Nuala McCarroll, Ms Anya Pierce, and Mr Diarmuid UaConaill to a 'Reception for Business Enterprise & Conference Ambassadors' in 2003. Following the reception in the garden, during which drinks and canapés were served, the President thanked all present, and those they represented, for their efforts in promoting Ireland in many different spheres.

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ACB Republic of Ireland Region News

Alan Balfe, Hon. Secretary

New Member: We welcome Ms. Alison Griffin, B.Sc., a biochemist working in Beaumont Hospital, as a new member of the ACB, in our Region.

Region Committee: At the AGM last April, the following were elected to the Committee: Dr. Tom Smith (Chairman), Dr. Alan Balfe (Hon. Secretary), Dr. Mark Kilbane (Hon. Treasurer), Paula O'Shea (Trainees' Representative). Continuing in office are Olwyn Lanigan (Regional Representative to Council), Dr. Peadar McGing (Regional Tutor) and Rowland Reece (Ordinary member). Another Ordinary member is to be co-opted, and an ACBI liaison member is to be appointed.

Minutes of ACB Council meetings are to be available to the membership on the ACB website after 3 months. Council wants to devolve a lot of work to the Region Committees, and to raise the profile of the regions and ensure they have adequate support.

Dr. Trevor Gray, Chair of the R.C.Path. examiners, will meet the ACBI training course participants, at Malahide on Thursday 13th November, the afternoon before ACBI 2003.

Regional Website: Council has decided that the Regions should set up their own website domains, in order to provide information to regional members. It is proposed that a single theme be adopted across all the region websites so that they all look similar, and that the approach already taken by the West Midlands Region (www.acbwm.org.uk) would work for each of the nine regions. We have chosen Rowland Reece, Principal Biochemist at St. Vincent's University Hospital, to be our site administrator when the project gets under way.

WANTED: New Representative to Council! Our current representative, Olwyn Lanigan, will complete her three year term next Spring. The AGM to be held in April will elect a Representative for the next three years. So, interested candidates, now is the time to start being interested! Further information can be obtained from Olwyn, or through any member of the Committee.

Dates of forthcoming Council meetings in London: 4 March 2004; 8 July 2004; 7 October 2004.

In the literature

Rhodes JS, Van Praag H, Jeffrey S, Girard I, Mitchell GS, Garland T Jr, Gage FH. Exercise increases hippocampal neurogenesis to high levels but does not improve spatial learning in mice bred for increased voluntary wheel running Behav Neurosci. 2003 Oct;117 (5):1006-16.

This study suggests that specially bred "exercise addicted" mice

demonstrate impaired learning compared to their non-running relatives. Yet another excuse to put the feet up.

Sherwood P, Lyburn I, Brown S, Ryder S. How are abnormal results for liver function tests dealt with in primary care? Audit of yield and impact. BMJ. 2001;322(7281):276-8.

The authors demonstrated that

"an important minority of patients with abnormal test results for liver function discovered by their doctor were not adequately investigated, resulting in missed treatable and sometimes communicable chronic liver disease." Patients with persistently raised LFTs should be referred to the appropriate consultant. It seems obvious but it doesn't always happen.

Report on IEQAS Conference 2003

by Rowland Reece

The 11th annual IEQAS Participant's Conference took place, as usual, in the Red Cow Inn on October 16th. The meeting was well attended with over 135 delegates and began with an opening address by Hilary Coates from the Irish Society for Quality and Safety in Healthcare (ISQSH). This group is now part of a wider European network and promotes Total Quality Management and transparency in patient care. It is an organisation we, as professionals in healthcare, should be liaising with more closely.

Hazel Graham, Operations Manager, then presented her annual review. 2003 saw the introduction of improved software and presentations, increased networking, particularly with user problems, with other EQA schemes and diagnostic suppliers. 2004 plans include a specialist review panel for myocardial markers through LabQuality, training workshops and the introduction of CRP.

The Plenary workshop was on a topic of concern to all, Accreditation. A panel of speakers from Crumlin and St.James' Hospitals gave their experiences of preparing for and having CPA inspection. This was very well received and many tips were being gratefully

jotted down for future use.

The following workshops then divided into two groups, Haematology and Clinical Chemistry. The Chemistry session focussed on the clinical impact of laboratory medicine on the treatment of Diabetes Mellitus (DM). Dr. Gerard Boran first gave an overview of the investigations important for the diagnosis of DM, the assessment and monitoring of long-term complications with particular emphasis, of course, on HbA1c.

Prof. John Nolan then discussed the huge problems we face with the exponential rise in new DM cases. The clinical viewpoint has now moved away from the management of end-stage complications, although still very important, towards detection of 'pre-diabetes' and intensive management of early DM. Key markers advocated were HbA1c, lipids, urinary albumin, insulin and c-peptide. Potential predictive markers such as GAD antibodies could also prove useful. Tight control, evidenced from DCCT and UKPDS trials, requires standardisation of HbA1c results. Prof. Nolan pleaded for all laboratories in the country that provide HbA1c monitoring to standardise their results and IEQAS is very active in this regard,

working with users and manufacturers.

Dr.Ned Barrett spoke about the methodologies of HbA1c measurement and the DCCT/IFCC standardisation. He outlined the performance of various systems for measuring HbA1c and showed that reduction in between-lab variability is continually improving. IFCC standardisation should bring all the labs even closer together and Dr.Barrett elucidated on the relationship between DCCT and IFCC values, noting that IFCC results will be lower, especially at lower values of HbA1c.

Des Kenny then spoke about reporting conventions for HbA1c and the dilemma facing labs in whether to report the molecularly correct HbA1c result, traceable to a reference method and calibrator (IFCC), or the clinically important DCCT values. We can either establish the relationship between the two and phase in IFCC, or calibrate against IFCC and recalibrate and report in DCCT, i.e. anchored to IFCC. The latter seems to be currently favoured. A recent proposal is being considered by the IFCC, that is to report IFCC values in different units to avoid confusion between old DCCT and new (lower) IFCC

(Continued on page 4)

values, such that a value of 3.4% would be reported as 34 mmol/L IFCC. The IEQAS steering committee supports this proposal.

After lunch, (very nice too), there was a general discussion on the tests we do, utility and workload and the ethics of adding on tests. A panel led this. Frank Clarke, DIT, spoke about the problem of providing tests which may not be clinically useful; should we stop doing obsolete tests, and be controlling expensive tests? John Brady, Crumlin, discussed the problems of increasing workloads, and

ways of managing and even reducing them. The topic of the ethics of adding on tests from the laboratory was introduced nicely by Ned Barrett with a typical real-life scenario and he went on to show results from a small survey carried out on users of his own service about their views on add-on tests.

Finally in this session Des Kenny briefly spoke about the recent and ongoing controversy regarding the IVD directive, CE marking and 'in-house' assays. This has been extensively covered in the latest ACB news, but Des said that the MHRA

interpretation of the legal viewpoint put forward would be challenged.

The last speaker was Alan Carr who gave a brief update on the new reporting format. Many users are now availing of the web service, including yours truly, who find it easy to use and get nice colour presentations- good for multiple analysers.

All in all, it was a very good meeting. Congratulations to the organisers. Hazel Graham said next year's meeting might be held outside Dublin – I thought it always had been!

Members' Publications

O'Hara, *Cavanagh N*, Cassidy M, Cullina M. The Role of transferrin saturation as a screening test for hereditary haemochromatosis in an Irish population seeking medical care. *Ann Clin Biochem* 2003 Mar;40 (part 2):169-174.

O' Shea C, McKie N, Buggy Y, Duggan C, Hill AD, McDermott E, O' Higgins N, Duffy MJ. Expression of ADAM-9 mRNA and protein in human breast cancer. *Int J Cancer* 2003 Jul 20 ;105(6):754-61.

Gurr E, Koller U, Blaton V, Lund E, Harmoinen A, Zerah S, Rizos D, Kenny D, Pazzagli M, Opp M, Willems H, Reguengo H, Queralto J, Wallinder H, McMurray J, Jansen R, Parviainen M, Beastall G, Kohse KP; European Communities Confederation

of Clinical Chemistry and Laboratory Medicine (EC4), EC4 Register Commission. The European Register for Specialists in Clinical Chemistry and Laboratory Medicine: guide to the Register Version 2-2003 and procedure for re-registration. *Clin Chem Lab Med* 2003 Feb;41(2):238-47.

Suliman AM, Smith TP, Gibney J, McKenna TJ. Frequent misdiagnosis and mismanagement of hyperprolactinemic patients before the introduction of macroprolactin screening: Application of a new strict laboratory definition of macroprolactinemia. *Clin Chem* 2003 Sep;49(9):1504-1509.

Accompanying editorial by M Fahie-Wilson on page 1434.

Members' News

The past year or so has seen a raft of clinical biochemist's positions either filled or in the process of being filled. Newly appointed positions in St Vincent's Hospital are Barbara Murray and Rowland Reece (Principal Grade), Paula O'Shea (Senior Grade), and Myra O'Kane (Basic Grade). In addition, vacant Principal Grade positions have been advertised for Beaumont Hospital and the Drug Treatment Centre, Pearse Street. In Cork University Hospital two Senior Biochemist posts are to be filled.

2003 NOBEL PRIZE

This year's Nobel Prize in Physiology and Medicine has gone to Paul C Lauterbur and Sir Peter Mansfield "for their discoveries concerning magnetic resonance imaging". In the early 1970's Lauterbur discovered the possibility of creating a two-dimensional image by introducing gradients in the magnetic field. Later Mansfield further developed the use of these gradients and showed how the signals could be mathematically analysed, which made it possible to develop a useful imaging technique. He also showed how extremely fast imaging could be achieved, a theory that became technically possible within medicine a decade later. More than 60 million investigations with magnetic resonance imaging (usually referred to as MRI) are performed worldwide each year. It is particularly useful for brain imaging, but has also found application for diagnosing multiple sclerosis, identifying the causes of lower back pain, and assisting in diagnosis, treatment, and follow-up of cancer. The award, however, is not without controversy (what's new?!). An American scientist, Raymond Damadian, claims that he 'invented' MRI before Lauterbur began his work, and should have shared in the prize. Damadian joins a long list of aggrieved scientists who feel they were unfairly treated by the Nobel Committee.

IFCC and EC4 News

The October/November online issue of IFCC News can be viewed at <http://www.ifcc.org/news/octnove2003/>. Among the topics that can be found is an editorial entitled *Progress and process: the clinical laboratory sciences in tomorrow's Europe*. In addition, reviews of this year's Focus meeting, and the AACC's annual meeting are here. An interesting history of the Spanish Society of Clinical Chemistry is presented and recent IFCC publications are highlighted. The latter includes references for the *Working Group on Standardization of HCG*

Measurements, and the *Committee on Plasma Proteins*.

The EC4 web site (<http://www.e-c4.org/>) contains a list of working groups ranging from Guidelines for Number of Consultant Clinical Chemists to the ISO and CEN Committees (the latter chaired by Des Kenny). The **EC4 Strategic Plan 2002-2005** is also here. An informative document called *Essential Criteria for Quality Systems of Medical Laboratories* can also be found.

Impact Factors

Scientific journals have not escaped the urge to categorise everything as 'best of'. Impact factors are the academic equivalent of Top of the Pops and to be published in a high impact factor journal does have certain kudos, not least in the pursuit of grants and tenure. A journal's impact factor is based on the number of times that articles in a journal are cited in the two years following the year of publication. To give an example the impact factor for *Science* in 1995 (21.911) was calculated as follows: Citations of 1995 articles published in 1993: 24,979; in 1994: 20,684. Total =

45,663.

Number of articles published in 1993: 1,030; in 1994: 1,054. Total = 2084. Impact factor = number of citations/ number of articles (45,663/2,084) = 21.911. This means that papers published in *Science* in 1993 and 1994 have been cited about 22 times in 1995 on average. Despite considerable reservations in the validity of impact factors they are not going to go away. For those interested here are the top ten clinical biochemistry related journals for 2001: *Clinical Chemistry*, *Laboratory Investigation*, *Journal of Molecular Medicine*, *Critical*

Reviews in Clinical Laboratory Science, *Seminars in Diagnostic Pathology*, *Journal of Laboratory and Clinical Medicine*, *Advances in Clinical Chemistry*, *Molecular Diagnosis*, *Archives of Pathology and Laboratory Medicine*, and *Clinical Biochemistry*. The *Annals of Clinical Biochemistry* are 11th, and *Clin Chim Acta* are 13th. The top rated journal, *Clinical Chemistry*, had an impact factor of 4.261 which means that papers published in 1999 and 2000 were cited 4 times on average in 2001. The 10th rated journal had an impact factor of 1.327.

Case Study

Peadar McGing



A 33 year old woman was referred from her GP to the A&E Department during the late afternoon. The GP's letter stated that she had presented to the surgery with a history of frontal headache for about 24 hours. She had been vomiting during the night and this had continued during the day. She had a small petechia rash on her right elbow crease, but no photophobia or neck stiffness. The GP's impression was 'no meningism, ?encephalitis'.

Preliminary lab tests included:

Na = 136 mmol/L, K = 3.0 mmol/L, C l = 99 mmol/L, TCO₂ = 22 mmol/L, Urea = 3.6 mmol/L, Creat = 66 µmol/L.

Hb = 14 g/dl, Plt = 217, wcc = 24.54 (4-11), neutrophils = 22.14 (2.0-7.5); INR = 1.8.

Glucose = 7.5 mmol/L.

She was seen by the Medical SHO on call who took the history again.

BP = 120/72, HR = 82 regular, Temp = 36.5 (but ?38 in GP's)

He ordered other tests including adding liver and bone profiles. The only abnormal results were Glob = 40 g/L, Bilirubin = 24 µmol/L. Normal results included PO₄ = 0.73 mmol/L and Alb = 36 g/L

Q1. Explain the abnormal results seen.

Q2. What other tests would you expect to have been ordered and what results might you anticipate?

Answer on page 7

Industry News

Clement Fitzgerald, Sales and Marketing Director of Randox Laboratories, has become the new Chairman of the British In Vitro Diagnostics Association (BIVDA). He will hold the position for two years.

The BIVDA website has an article by Prof Chris Price (President of the ACB) on the benefits of in vitro diagnostic testing and its impact on clinical outcome (<http://www.bivda.co.uk/news/index.cfm?ccs=116&cs=742>).

The site also has a position paper on osteoporosis and the role of in vitro diagnostics in monitoring and detecting this condition (<http://www.bivda.co.uk/documents/index.cfm?cl=4&cls=1>).

Public Library of Science

A couple of years ago I wrote about an initiative called the Public Library of Science (<http://www.plos.org/index.html>). Its aim was to encourage the publication of all scientific journals free on the web. To date only a handful of journals are doing this but many provide free access to their content after a period ranging from six months to two years. For a comprehensive listing of journals providing totally free or time delayed access check out High

Wire Press's excellent website (<http://highwire.stanford.edu/>). Individual articles can be searched for and the returns indicate whether they can be viewed immediately or only after payment of a charge. This site can consume serious amounts of your time.

Getting back to the Public Library of Science, the founders have launched the first of two freely available online journals. They did this, they say, to prove that high quality, peer-reviewed journals can be successfully published free on the web. The initial offering is called PLoS Biology (issue one available at <http://www.plosbiology.org/plosonline/?request=index-html>). The rationale for this development is discussed in an editorial in the first issue. A second journal, PLoS Medicine will be launched in mid 2004.

ACBI – We're Not the Only Ones!

by Alan Balfe

ACBI. Initials familiar to us all, they evoke immediately in us a sense of our professional identity. The Association of Clinical Biochemists in Ireland is our organisation, our collective statement of a commitment to excellence in our work. The work of the ACBI is something of which we can be proud – work with many facets including representing us and contributing to the work of the IFCC and EC4, organising and supporting training, making representations to the DoHC, producing guidelines on the use of laboratory tests, organising scientific meetings, including our Annual Conference with its reputation for high quality over the years.

But there are many other ACBIs. To many other groups around the world, the initials ACBI mean something entirely different. Enter the term in an internet search engine, and discover a world of other identities. Firstly, we should mention the Association of Clinical Biochemists of India. The Indian association was established in 1975, eleven years after our association was founded, and will hold its 30th Annual Conference at Bangalore next January. Also in the scientific arena, there is the Association of

Consultants to the Bioscience Industries, founded in 1990 in the U.K. In Ireland, there are the Associated Craft Butchers of Ireland, set up in 1999 to develop and promote the interests of surgeons (no, family butchers). If you were an ACBI member in the Middle East, you might belong to the Association of Contractors and Builders in Israel. Returning to India, you will find the Association of Cricket for the Blind in India, which surely must be an inspirational endeavour. In the USA, there is the American Council of the Blind, and its Indiana affiliate, the ACBI. If you want a career change, you could go to the Phillipines, and join the Association of Coconut Brokers, Inc. Come back to France, where you will find the Agence Commerciale Bourgogne Industrie, or the Association Citizen Band Independente. Go on to Italy to meet the Associazione Culturale dei Banaadiri in Italia.

This has been but a brief, if far-ranging, tour. Make your own tour, when you need to escape the frustrations of life as a clinical biochemist in the Irish health system. There are many options available, and you can still be a proud ACBI member!

Case Study Answer

[This case is one previously used for the Mater Hospital Biochemistry Case Meeting. The opinions are those of the author, post appropriate consultation. Opinions from readers of this case are welcome (to pmcging@mater.ie)]

The SHO noted the following as presenting complaints: Myalgia and arthralgia x 30hrs. Frontal headache x22hrs, worsening over time and now patient crying with pain. Vomiting during night + today. Photophobia but no neck stiffness. Petechial non-blanching rash on right arm. No seizures or confusion. GCS on admission 15/15 but dropped to 11/15. CT brain – no bleed, no focal neurology. Impression – (1) Meningitis, (2) ?DIC. A lumbar puncture was ordered which was recorded as “completely atraumatic tap” giving turbid fluid.

CSF biochemistry:

glucose = 0.2 mmol/L, protein = 5570 mg/L.

CSF microbiology (for sample 1, samples 2&3 similar):

Appearance = cloudy, rcc = 70/μL, wcc = 11000/μL, xanthochromia = absent; Gram stain: gram negative diplococci (?Neisseria), Leishman: 100% polymorphs.

Remarks: PCR for Neisseria meningitidis = Positive (result not available on call but can be ready within 24 hours).

The patient was treated with IV antibiotics, dexamethasone, and fluids (saline and Hartman's).

Less than 48 hours after her initial presentation to the hospital she was feeling well with only a mild residual headache. She was kept in hospital until she completed a two week course of her antibiotics.

In respect of her presenting biochemistry:

Hypokalaemia could be due to her vomiting but of itself vomiting usually causes metabolic alkalosis whereas this patient has a low normal TCO₂ (=22 mmol/L). What seems most likely to be happening here is that she has a metabolic acidosis as a result of septicaemia which is offsetting the milder alkalosis associated with vomiting.

Mild hyperbilirubinaemia is most likely due to fasting for the duration of the vomiting. 36 hours later it was back in the reference range (=16 μmol/L).

Mild hyperglycaemia is likely just a response to her illness.