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Advance Notice of ACBI 2009

Thomas Carroll (Alpha One Foundation, RCSI/Beaumont Hospital) being presented with the Geraldine Roberts Memorial Medal for best poster presentation at ACBI 2008
From the President

Focus on Quality – our Professional Commitment

With the current public interest in regulation and quality in the healthcare field, it was fitting that Dr. Tracey Cooper, Chief Executive of HIQA (the Health Information and Quality Authority) accepted the invitation to deliver the keynote address at the opening session of ACBI 2008, our annual conference. The following is an excerpt from my opening address, before introducing Dr. Cooper:

“…… Speaking at the recent meeting of IEQAS (the Irish External Quality Assurance Scheme for Clinical Laboratories), the Minister for Health and Children, Mary Harney, said that the Irish health sector was entering a new era where “standards would be the dynamic for making things happen”, an era of “quality driving change”. As we move towards a licensing regime, she said, HIQA will have the function of setting standards and ensuring they are enforced.

In our field, two central elements will be accreditation of laboratories and statutory registration of the laboratory professionals. The function of accreditation is to ensure the quality and fitness for purpose of the laboratory, while registration will ensure the quality and fitness to practise of the staff. The underlying purpose is protection of the public. The legislation has already been passed for State Registration of Clinical Biochemists and other healthcare professionals. There is currently no legal requirement for laboratory accreditation in this country. However, many public hospital laboratories have already been accredited, and many more are pursuing accreditation.

Historically, laboratories were set up in acute hospitals for hospital work. These laboratories evolved to provide services to local GPs, although not explicitly funded for this. Tests for GPs constitute a large part of the workload in bigger laboratories. There is now a proposal, in the unpublished Pathology Review conducted for the HSE, to take testing for GPs out of the public hospitals, and put it in three new stand-alone laboratories located around the country. We think this will cause fragmentation rather than continuity of services between the primary and secondary care settings. There is a good case for public hospital laboratories to be allowed to tender for provision of services to GPs, on a level playing field with any private institution. In our customer satisfaction surveys, GPs indicate a high level of satisfaction with the service they are currently getting.

There is also a trend towards provision of pathology tests at the point of care in the community. This can be more convenient for the patient, but it is vital that the quality and cost-effectiveness of this testing is assured. To provide leadership, the ACBI with the other professional bodies and the competent authority, the Irish Medicines Board, have produced guidelines for Point of Care Testing (POCT). This document deals with POCT in the hospital setting, but includes an outline framework for POCT in Primary Care and in Community pharmacies.

It should be recognised that Clinical Biochemists as a profession have a long-standing focus on quality. External quality assurance schemes were first developed and promoted in clinical biochemistry more than 40 years ago. This was well ahead of any other clinical field. Our own Irish scheme, IEQAS, evolved in 1981 from an internal scheme set up by the ACBI for its members in the 1970s.

At this conference last year, we marked the passing of our colleague Des Kenny. Des had a central role in the development of ISO15189, the international standard for Quality Management in the Medical Laboratory, which forms the basis for hospital laboratory accreditation.

Des was also involved in the development of the European Register of higher specialists in Clinical Biochemistry eleven years ago. In the absence of State registration in this country, the ACBI set up a voluntary register of Clinical Biochemists in 1998, underpinned by a code of ethics.

Our commitment to quality over the years can also be seen in the frequent inclusion of quality issues on the programme of this meeting. For example:
In 2007, Graham Beastall spoke on “Quality: what is it and why does it matter?”

In 2005, Andrea Horvath spoke on “What is the evidence base for biochemical testing?”

In 2003, we had Trevor Gray on “Clinical Governance”.

In 2002, there was a session on Quality Management, with presentations from world luminaries Callum Fraser, James Westgard, Jonathan Middle and David Burnett.

In 1999 there was a whole day on the “Application of Evidence Based Medicine in clinical biochemistry”.

In 1995 we had Nuala McCarroll on “Accreditation and total quality management” and Stephen Halloran on “Clinical Audit”.

In 1990 Des Kenny spoke on “International standards in the Clinical Laboratory”, Jim Westgard was also with us in 1987 and spoke on “General Principles of Quality Management” and on “Quality Control Procedures for Clinical Chemistry Assays”.

We have also concerned ourselves with the quality of information available. The ACBI has produced and published a series of Guidelines for users of the laboratory service. Topics covered to date in these guidelines are the Use of Tumour Markers, the Use of Therapeutic Drug Monitoring and the Use of Biochemical Cardiac Markers and Risk Factors......

In her keynote address, we heard Dr. Cooper speak very positively about the professional commitment to laboratory quality she witnessed in her visits to healthcare facilities over the past year. This recognition is an encouraging counterbalance to the cloud under which hospital laboratories have laboured for the past two years.

This cloud was cast by the public pronouncements from another quarter in the HSE. It was stated through the broadcast media that most Irish hospital laboratories were not accredited. This was stated in such a way as to imply rather disingenuously that laboratory quality was generally suspect. There was no acknowledgement of the existence of quality control and quality assurance programmes. It was not revealed that there is currently no legal requirement for laboratory accreditation in this country. It was not revealed that no formal proposal had been brought forward by the HSE for public laboratories to achieve accreditation, nor had resources been budgeted for this. Was there not something hypocritical about this approach? Does not the same attitude pervade the lack of transparency surrounding the status of the Pathology Review prepared by Teamworks for the HSE more than one year ago? On the evening of our conference, the HSE responded to its coverage on RTE News with a statement declaring that the Review would be published in a few weeks. As you read this the Review has not yet been published.

Alan Balfe
President
Association of Clinical Biochemists in Ireland
Further Commentary on the National Academy of Clinical Biochemistry (NACB): Biomarkers of Heart Failure

Dr Sean Cunningham, St Vincent’s University Hospital

The NACB Guidelines for Utilisation of Biochemical Markers in Acute Coronary Syndromes & Heart Failure, published during 2007, was the subject of a previous commentary in the April 2008 edition of this newsletter. The previous commentary covered recommendations for the use of biochemical markers for diagnosis of myocardial infarction, problematical areas such as chronic renal failure and percutaneous coronary intervention, biochemical markers of ischaemia, early risk stratification and point of care testing. In this further commentary, the sections of the guidelines dealing with clinical utilisation of cardiac biomarker testing in heart failure and related analytical issues are considered. The full guidelines are available on the NACB website (www.aacc.org/AACC/members/nacb/lmpg/) and were published in chapters in Clinical Chemistry and Circulation Journals during 2007.

Background

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricles to fill with or eject blood. It is estimated that only 50% of heart failure patients survive up to 4 years. It is a growing problem, affecting 2 – 3% of the total US population. The increasing prevalence of heart failure is due to the aging population, as well as the marked increase in survival of patients who have suffered myocardial infarction.

The diagnosis of heart failure is a clinical diagnosis based on signs and symptoms, rather than any stand-alone test result. However, the diagnosis may be difficult, particularly in the primary care setting and in patients presenting acutely to the emergency department. Therefore, clinical biomarker testing can play a role in the evaluation of patients for heart failure, in particular to confirm the presence or absence of the heart failure syndrome. The natriuretic peptides, particularly BNP and its amino-terminal co-metabolite (NT-proBNP) have proved the most useful biomarkers to date. However, various other neurohormone, inflammatory, metabolic and other biomarkers are currently under study in the setting of heart failure. (For list, see Table 3.1 in the Guidelines).

BNP production is augmented primarily by increase in wall tension in response to pressure and volume overload in both the atria and the ventricles. Therefore, elevated blood BNP and NT-proBNP occur in the setting of elevated filling pressures in patients with cardiac dysfunction and can provide relatively reliable diagnostic and prognostic information. Blood natriuretic peptide levels are reduced following long-term treatment with ACE inhibitors and angiotension II receptor blockers and spironolactone. A wide variety of clinical factors have been shown to influence blood natriuretic peptide levels including age and sex, renal function, body habitus, thyroid function and anaemia. Natriuretic peptides are higher in women than men and increase with age. Obesity has been associated with lower blood levels of BNP and NT-proBNP and levels should be interpreted with caution, especially in ruling out cardiac causes of dyspnea. Renal impairment has been shown to increase NT-proBNP concentrations and to increase BNP to a lesser extent.
Recommendations for the use of biochemical markers for diagnosis of heart failure

1. In the acute setting, BNP or NT-proBNP testing can be used to rule out or to confirm the diagnosis of heart failure among patients presenting with ambiguous signs and symptoms (Class I, level of evidence A)

2. In the non-acute setting, BNP and NT-proBNP testing can be helpful to exclude the diagnosis of heart failure among patients with signs and symptoms suspicious of heart failure (Class IIa, C)

3. In diagnosing patients with heart failure, routine blood BNP or NT-proBNP testing in patients with an obvious diagnosis of heart failure is not recommended (Class III, C) In diagnosing patients with heart failure, blood BNP or NT-proBNP testing should not be used to replace conventional clinical evaluation or assessment of the degree of left ventricular structural or functional abnormalities (e.g. Echocardiography, invasive haemodynamic assessment)(Class III, C)

The strongest evidence for the use of the natriuretic peptides in diagnosis of heart failure is in the acute setting, in the evaluation of patients with acute dyspnea e.g. the “Breathing Not Properly” study for BNP, the PRIDE study for NT-proBNP (Maisel A.S et al, NEJM 2002; 347:161 – 7 and Januzzi et al, Am J Cardiology 2005; 95: 948 – 54 respectively).

The use of the natriuretic peptides in diagnosis of heart failure in the non-acute primary care setting remains to be established and their use is likely to be mostly in the rule-out of heart failure. In this setting particularly, there are difficulties with age specific reference ranges and cut-offs.

At this time, natriuretic peptide testing should still be considered only as part of the diagnostic evaluation in heart failure, and not the diagnostic definition. Clarification and agreement on the rule in and rule out cut-off’s for various clinical scenarios is needed for the heart failure field to advance.

Recommendations for use of Biochemical Markers for Risk Stratification of Heart Failure

1. Blood BNP or NT-proBNP testing can provide a useful addition to clinical assessment in selected situations, when additional risk stratification is required (Class IIa, A)

2. Serial levels may be used to track changes in risk profiles and clinical status among patients with heart failure in selected situations where additional risk stratification is required (Class IIa, B)

The ACC/AHA Guidelines for the management of chronic heart failure state that a large majority of patients who develop heart failure may have proceeding structural cardiac abnormalities that can be recognised before disease progression. However, there have been inconclusive data regarding the role of screening for asymptomatic left ventricular dysfunction using natriuretic peptide testing in several studies.

It may be more useful and cost effective to focus on high-risk sub-groups for heart failure screening. Such high-risk groups include those with a history of hypertension, diabetes mellitus, coronary artery disease, and also the elderly. It is possible that blood natriuretic peptide testing
may be useful for screening those high risk populations who may otherwise be referred for further echocardiographic screening for asymptomatic left ventricular dysfunction (ALVD).

Prospective studies are needed to establish evidence for stratifying patients according to natriuretic peptide levels.

**Recommendations for the use of Biochemical Markers in guiding Management of Heart Failure Patients**

1. *Routine Blood BNP or NT-proBNP testing is not warranted for making specific therapeutic decisions or patients with acute or chronic heart failure because of the still emerging, but incomplete data as well as intra and inter-individual variations (Class III, B)*

Two studies have found benefits from titrating therapy with ACE Inhibitors and diuretics to achieve a target NT-proBNP Level, while others have not. The wide variation of single or sequential blood natriuretic peptide levels in chronic heart failure after long-term medical therapy has limited the usefulness of these markers. Until the results of current prospective studies are assessed, routine blood BNP or NT-proBNP testing is still not warranted for therapeutic decisions in patients with heart failure.

**Overview of analytical issues for Heart Failure Biomarkers**

These NACB Guidelines are the first international recommendations addressing the analytical aspects of BNP and NT-proBNP for clinical use in heart failure.

**Recommendations for Analysis of Biochemical Markers of Heart Failure**

1. *Before introduction into clinical practice, BNP and NT-proBNP assays must be characterised with respect to the following pre-analytical and analytical issues:*
   - Pre-analytical issues include sample type and appropriate blood collection tubes, together with the effects of storage time and temperature.
   - Analytical issues include identification of antibody recognition epitopes, description of the calibration material used (in particular with respect to assignment of values), determination of cross-reactivity characteristics (especially in regard to related natriuretic peptides), evaluation of the dilution response and evaluation of interferences such as from heterophilic antibodies, rheumatoid factors, human antimouse antibodies, etc. (Class I, C)

The issues raised are most likely to be addressed by the manufacturers of commercial assays but clinical laboratories using these assays should satisfy themselves that the appropriate evidence exists.

2. *Results for both BNP and NT-proBNP should be reported in µg/L rather than pmol/L until assays and calibrants have been better defined. (Class I, C).*
3. *Upper Reference Limits at the 97.5 percentile of the reference value distribution, should be independently established for both BNP and NT-*
proBNP based on age, by decade and by gender (for each commercial assay) (Class I, C).

4. Harmonisation of BNP Assays is needed for instance in respect of the diagnostic cut-off levels, whereas for NT-proBNP, for which there is only one source of antibodies and calibrators, harmonisation of assays should not be a problem.

5. ROC Curves should be established to evaluate the clinical effectiveness and to establish optimal medical decision cut-offs for both BNP and NT-proBNP assays for diagnostic usefulness (Class I, C).

6. Assays should have a total imprecision (% CV) of <15% at concentrations corresponding to their age and gender defined upper reference limits (Class IIa, C).

7. Caution should be exercised in interpreting changes of < 50% in relation to medical therapy because of high biological variation for both BNP and NT-proBNP.

Other considerations

Recombinant BNP therapy will cross-react in the BNP assay but not in the NT-proBNP assay. There is currently conflicting evidence regarding the specificity of the natriuretic peptide assays in regard to related peptides.

Specimens for BNP require EDTA anti-coagulated whole blood or plasma collected in plastic tubes. Samples should be collected in ice tubes and processed rapidly to avoid in-vitro degradation. For NT-proBNP, serum or heparin plasma may be used and either glass or plastic tubes are acceptable.

*Footnote:* In these Guidelines, the strength of scientific data supporting each recommendation in characterised using the scoring criteria adopted from the American Heart Association/American College of Cardiology. In this system, recommendations are designated Class I if based upon evidence and/or general agreement that a given procedure or treatment is effective, IIa or IIb if there is conflicting evidence and/or divergence of opinion about its effectiveness and Class III if there is evidence and/or general agreement that it is not effective. Level A recommendations are based on the strongest evidence e.g. from RCTs, Level B are based upon smaller studies and Level C recommendations are based mainly on expert consensus.
In lipid research there has been much debate over the practical utility of the dietary ratio of n-6 to n-3 polyunsaturated fatty acids (PUFAs) in optimizing the benefits of n-3 fatty acids (C18-C22) on cardiovascular health. A review from February 2008 (Current Opinion in Lipidology, 19(1):57-62) should help to settle any outstanding controversy over this ratio. This review examined the supporting evidence from the OPTILIP study (American Journal of Clinical Nutrition, Vol. 84, No. 6, 1290-1298, December 2006). It reinforced current recommendations to increase the consumption of the preformed PUFAs eicosapentaenoic acid (EPA) and docosahexaenoic (DHA) acid in fish. It also supported dietary measures to increase intake of α-linolenic acid and to decrease intakes of linoleic acid, to promote the endogenous synthesis of these longer chain n-3 PUFAs.

The question of whether the ratio of n-6/n-3 PUFAs or total amounts of dietary PUFAs is of more importance to cardiovascular health has been addressed recently in both the randomly controlled OPTILIP trial and in a stable isotope tracer study (American Journal of Clinical Nutrition, Vol. 84, No. 1, 44-53, July 2006). The OPTILIP study concluded that lowering the n–6/n–3 ratio by increasing the intake of n–3 PUFAs decreases both fasting and postprandial plasma triglyceride concentrations and results in favourable changes in LDL size in older men and women; however it does not influence fibrinogen, factor XIIa, or indexes of factor VII (two of the central proteins in the coagulation cascade).

Lowering the n–6/n–3 ratio by increasing the intake of α-linolenic acid and decreasing that of linoleic acid affected neither plasma triglycerides nor hemostatic variables. OPTILIP concluded that lifestyle factors, such as high BMI, alcohol intake, cigarette smoking, and the fat content of a meal, are significant determinants of these haemostatic factors.

These two studies were independently unanimous in concluding that the ratio of n-6/n-3 PUFAs is of no value in modifying cardiovascular disease risk. The latter study (American Journal of Clinical Nutrition, Vol. 84, No. 1, 44-53, July 2006) also showed that the absolute amounts of dietary linoleic acid and α-linolenic acid are of relevance to the efficiency of conversion of α-linolenic acid to eicosapentaenoic acid and docosahexaenoic acid. The amounts of α-linolenic acid linoleic acid in the diet, but not their ratio, determine α-linolenic acid conversion.

Linoleic acid, the omega-6 fatty acid, is found in vegetable oils such as sunflower oil. Seed oils are the richest sources of α-linolenic acid, notably those of rapeseed, soybeans, walnuts and flaxseed. Green vegetables are also a good source of α-linolenic acid.

Fish oils are rich in DHA. Most of the DHA in fish and more complex organisms originates in photosynthetic and heterotrophic microalgae, and becomes increasingly concentrated in organisms as it moves up the food chain.

EPA is obtained in the human diet by eating oily fish or fish oil.

There is not enough information available to set a safe upper limit for omega-3 fatty acids. The Food and Drug Administration says up to 3 grams per day of EPA and DHA combined is generally recognized as safe. DHA and EPA may have negative effects on the immune system and may inhibit blood clotting, so supplementation should only be done with caution.


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Human Anatomy Online
http://www.innerbody.com/
Educational site detailing the anatomy of the human body. Lots of graphics and clickable descriptive links.

Views of the Solar System
http://www.solarviews.com/eng/homepage.htm
Excellent multimedia resource for information on the solar system and beyond. Great images and graphics.

DNA from the Beginning
http://www.dnaftb.org/dnaftb/
As it says on the home page this is an animated primer on the basics of DNA, genes, and heredity. Key concepts of genetics are explained using animation, image galleries and video interviews. Kept at a fairly basic level but impressively done nonetheless.

TED: ideas worth sharing
http://www.ted.com/
Lectures available online from notables involved in technology, entertainment and design (and a lot of side-shoots). A recent addition is a lecture by Kary Mullis on what scientists do - very entertaining.
and ACBI 2009 is already in the planning stages so this is a good time to reflect on this year’s conference.

The conference began in the full blaze of TV lights as RTE’s Health Correspondent Fergal Bowers captured the opening of the meeting. The news item was aired on the Six-One News and thanks to the Internet we were all able to enjoy watching the two-minute news segment prior to the Lab Are Vital launch on Saturday afternoon. The news piece can still be viewed at http://www.rte.ie/news/2008/1017/6news.html. Scroll down to the piece marked ‘Concern over hospital lab tests. Fergal Bowers, Health Correspondent, reports that biochemists are concerned about plans to block GPs’ access to public hospital laboratory tests.’ Segments of both the opening address by ACBI President, Dr Alan Balfe and the interview with Dr Tracey Cooper, CEO of HIQA are included.

The Irish Medical News was represented by their reporter Nick O’Donoghue who wrote a number of news articles focussing on the opening session The Impact of a Changing Ethnic Population on Clinical Biochemistry. A link from the ACBI website to these pieces can be established when the new archive section of the IMN website is in place.

ACBI were very fortunate to have Dr Tracey Cooper of HIQA give the Keynote Speech. She focused on the importance of quality and reliability in the laboratory and highlighted a number of key elements:

- Clinical governance and leadership,
- Communication between lab staff and direct care providers,
- Adaptability to service needs,
- Guidelines for collecting and evaluating samples,
- Ongoing review of rejected and misinterpreted specimens,
- Effective audit of proficiency,
- Quality assurance plus accreditation for both individuals and institutions.

There were a variety of lectures from these opening talks right through to the closing lecture from Dr Danielle Freedman on Clinical Biochemistry Tests in A&E. Subjects covering the topical areas of biochemistry for the elderly and laboratory aspects of heart failure and organ transplantation were also discussed.
The 32nd annual conference of the Association of Clinical Biochemists will be held on Friday 16 and Saturday 17 October 2009 in the centre of Dublin at the Radisson SAS Hotel Golden Lane, Dublin 8.

Conference topics
Fluid biochemistry
Laboratory medicine and nutrition
Endocrinology and nephrology
Biochemistry for the future - managing resources

Additional information and booking forms will be available from the ACBI website www.acbi.com
email: acbiconference@gmail.com

Congratulations to Thomas Carroll of Beaumont Hospital who was presented with the Geraldine Roberts medal by the President of ACBI Dr Alan Balfe for his poster titled ‘Prevalence of Alpha-1 Antitrypsin Deficiency in Ireland’.
The Friday evening in the Chester Beatty Library was an opportunity to sample this delightful treasure of our capital city, a visit that many delegates had long considered. The conference finished on Saturday evening with the ACBI Annual Dinner, again a most enjoyable night. Speaking of 2009, we did get good feedback from delegates but if you have had more suggestions since the meeting please pass them on by email to acbiconference@gmail.com.
We would also like to hear from anyone who is a member or who would be a regular attendee at ACBI conferences but who didn’t attend this year – was there any reason for your absence that we might address for 2009?
Finally my personal thanks go to our Corporate Members, without whose support we couldn’t hold a conference at this level, our speakers, chairpersons and poster authors, and all our delegates, who made the conference a very special event.

Peadar McGing.
A giant step forward not a leap of faith

Your training needs are always moving forward. That’s the inspiration behind our new cobas academy: a whole range of training packages to support you in the use of IVD systems and services provided by Roche Diagnostics.

cobas academy includes our comprehensive, secure ID-guaranteed e-learning facility, designed to monitor and refresh operator competence.

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Plus, with the forthcoming opening of our new, state-of-the-art training facilities, we can continue to provide progressive training and support at a pace (and place!) to suit you – every step of the way.

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