**News** 

# Clinical Biochemistry







Newsletter of the Association of Clinical Biochemists in Ireland

and the Association for Clinical Biochemistry and Laboratory Medicine (Republic of Ireland Region)



Dr. Jennifer Brady (President of the ACBI) and Prof. Tomris Ozben (President of the EFLM and President-elect of the IFCC) at ACBI 44

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Editors: Dr. Martin Healy; Dr. Peadar McGing

## Message from the President of the Association of Clinical Biochemists in Ireland Dr. Jennifer Brady

Since our last newsletter, we held a very successful conference in Cork. It was really wonderful to see so many of you there, to meet some of you for the first time and to hear a fantastic array of speakers. As the national society for both EFLM and IFCC, the ACBI recognises the importance of our close links with EFLM and IFCC. I was therefore really delighted to welcome our colleagues from EFLM and IFCC, Prof Tomris Ozben, Dr Pilar Fernandez-Calle and Dr Bernard Gouget to our conference. We also welcomed a number of the students from the latest class of the MSc in Clinical and Diagnostic Biochemistry in UCD, a course directed by Dr Graham Lee. I want to congratulate the students on their exam success and wish them the very best for their future careers.

I want to thank everyone who contributed to the conference by presenting posters and clinical cases, leading and chairing sessions, judging the competitions and providing sponsorship. It is this valuable input which makes the conference such a success. I want to congratulate once again the conference organising committee, Dr Séan Costelloe, Alison Bransfield, Caroline Joyce, Kelly Foley and Dr Briedgeen Kerr for all their excellent work up to and throughout the conference.

Further afield, it was great to see the ACBI well represented at a number of recent conferences including UKMedLab22, British Society for Genetic Medicine 2022 conference and the Irish Endocrine Society annual meeting in Dublin. A particular mention to Caroline Joyce from Cork who presented her research at the XXI World Congress on Gestational Trophoblastic diseases in Sydney.

The ACBI Council held our first face to face meeting in almost 2 years in Cork. Council remains busy representing our membership at various national and international forums. ACBI Council along with other professional bodies met with the Chair of the Group to inform the Strategic Direction of Laboratory Medicine to get an update on the work of this group. We expect to receive a draft report for consultation soon. Dr Séan Costelloe and I recently met with Dr Deirdre O'Brien, the Clinical Lead for the National Clinical Progamme in Pathology. We very much look forward to working with her and the new team at the programme office to deliver the progamme's strategic objectives. I am very pleased to say that the ACBI has joined the Health and Social Care Professions Alliance (HSCPA). The HSCPA seeks to promote the Health and Social Care professions as partners in the planning, management and delivery of Health and Social Care in Ireland. I am very grateful to Dr Graham Lee and Dr Heloise Tarrant who are representing the ACBI at this forum. The ACBI joined with other HSCP professional bodies in welcoming the announcement by Minister for Health Stephen Donnelly that a HSCP role is being created in the Department of Health. The ACBI position is that this role should be at the level of the Chief HSCP officer.

We have been working hard on getting our website updated so that it will have all the functionality we require in terms of membership applications and renewals, CPD and our conference. This has taken some time but we can see the end in sight and look forward to launching this improved website in the New year.

I want to congratulate Dr Peadar McGing on being awarded an honorary Fellowship of the ACB (Association of Clinical Biochemistry and Laboratory Medicine UK). Peadar was nominated by the ACB Republic of Ireland regional committee and his nomination was ratified at the ACB AGM during the summer. Peadar's award recognised his work on tumour markers, cardiac markers and of course the ACBI 'Biochemistry of Body Fluids' guideline which is renowned for its practical information and has recently been cited in the Tietz Textbook of Clinical Chemistry. He has led the Irish reference range harmonisation project and contributed to the training of Clinical Biochemists in Ireland for many years. Perhaps a distinguishing feature of the application was Peadar's contribution to raising the profile of Clinical Biochemistry with the public with his contributions to the Irish Medical News and The Medical Independent, the lay press and of course his many years as an editor of this newsletter. Peadar's recent poster at UKMedLab22 on the history of point of care testing drew significant interest and is testament to his dedication to preserving the history of Clinical Biochemistry. Chomhghairdeas leat on receiving this very worthy award and for flying the flag for the ACBI at home and abroad.

The ACBI and its members have long had a very close working relationship with our colleagues in the UK and the ACB. It was really lovely to meet many of those

colleagues at the recent UKMedLab22 meeting. The continued activity of the ACB Republic of Ireland region committee, and representation at the ACB Council, the Trainees committee and the Education committee are testament to that important interaction between us and our colleagues in the UK on common issues such as training and education. From January 2023 your ACBI membership comes with the additional benefit that you will be entitled to a reduced ACB membership fee. The fee will be £150 instead of the normal £240. This is a significant saving and we are grateful to the ACB for recognising our members in this way. I would encourage you to think about joining ACB if you have not already done so. There are many benefits including access to the Annals of Clinical Biochemistry, excellent webinars throughout the year, educational material on their website and reduced rates at their annual conference. See acb.org.uk for more information.

For those of you who are ACB members, the ACB Republic of Ireland region committee will be looking for new members at the upcoming AGM. Stepping down

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will be myself as chair, Karen Heverin as treasurer/ secretary and Alison Bransfield as ordinary member. This is an excellent opportunity to get experience on a committee which is really useful for your CV, and interact with colleagues in the UK. It is really important that ACB members step forward to keep this committee active. Nominations will be sought shortly.

Don't forget the ACBI mentoring programme for Clinical Biochemists is now available, information will be available shortly on the website, or get in touch with ACBI Council via the secretary email. Please avail of it if you would like support with your career progression and also get in touch if you are interested in becoming a mentor. Don't forget to follow us on Twitter **@ACBIrl** and tag us if you are attending an event or presenting a poster.

Finally, I want to wish you all a very happy festive season and a very prosperous 2023. I look forward to seeing you all again in 2023.



## **Recent Reviews of Interest**

Serum creatine has long been a staple of renal function but issues of assay standardisation continue to be debated

Pottel, H., Cavalier, E., Björk, J., et al. (2022). Standardization of serum creatinine is essential for accurate use of unbiased estimated GFR equations: evidence from three cohorts matched on renal function. Clinical kidney journal, 15(12), 2258–2265. Click for paper: 10.1093/ckj/sfac182

Clinical importance of serum magnesium increasingly recognised but reference intervals still not universally agreed

Rosanoff, A., West, C., Elin, R. J., ...MaGNet Global Magnesium Project (MaGNet) (2022).

Recommendation on an updated standardization of serum magnesium reference ranges. European journal of nutrition, 61(7), 3697–3706. <u>10.1007/s00394-022-02916-w</u>

## A review of the many factors that influence interpretation of HbA1c results

Chen, Z., Shao, L., Jiang, M., Ba, X., Ma, B., & Zhou, T. (2022). *Interpretation of HbA1c lies at the intersection of analytical methodology, clinical biochemistry and hematology (Review).* Experimental and therapeutic medicine, 24(6), 707. <u>10.3892/etm.2022.11643</u> Detailed historical and current review of the role of vitamin D, calcium and phosphate in the aetiology of rickets

Miller, W. L., & Imel, E. A. (2022). *Rickets, Vitamin D, and Ca/P Metabolism.* Hormone research in paediatrics, 95(6), 579–592. <u>10.1159/000527011</u>

## CCLM's role in highlighting the laboratory diagnosis of Covid-19

Favresse, J., Douxfils, J., Henry, B., Lippi, G., & Plebani, M. (2022). *Clinical Chemistry and Laboratory Medicine celebrates 60 years - narrative review devoted to the contribution of the journal to the diagnosis of SARS-CoV-2.* Clinical chemistry and laboratory medicine. Advance online publication. <u>10.1515/cclm-2022-1166</u>

## Evolution of troponins from specialised research in muscle contraction to its pivotal role in diagnosing myocardial infarction

Lackner K. J. (2022). *Cardiac troponins - a paradigm for diagnostic biomarker identification and development.* Clinical chemistry and laboratory medicine. Advance online publication. <u>10.1515/cclm-</u> <u>2022-1112</u>

## A Selection of Members' Recent Publications

Experience of women on the Irish National Gestational Trophoblastic Disease Registry. Joyce CM, Coulter J, Kenneally C, McCarthy TV, O'Donoghue K. Eur J Obstet Gynecol Reprod Biol.

2022 May;272:206-212. doi: 10.1016/ j.ejogrb.2022.03.039. Epub 2022 Mar 28

Reference intervals for clinical biochemistry and haematology tests during normal pregnancy. Groenendijk W, Bogdanet D, Dervan L, Finn O, Islam MN, Doheny H, Griffin TP, Blake L, Lyons M, Kilcooley M, Krawczyk J, Gilmore R, Griffin DG, Gaffney G, Dunne FP, **O'Shea PM.** Ann Clin Biochem. 2022 Oct 4:45632221128686. doi: 10.1177/00045632221128686. Online ahead of print

The role of early pregnancy maternal pGCD59 levels in predicting neonatal hypoglycaemia- subanalysis of the DALI study.

Bogdanet D, Luque-Fernandez MA, Toth-Castillo M, Desoye G, **O'Shea PM**, Dunne FP, Halperin JA; DALI Core Investigator Group. J Clin Endocrinol Metab. 2022 Sep 2:dgac498. doi: 10.1210/clinem/ dgac49

The Diagnostic Accuracy of Second Trimester Plasma Glycated CD59 (pGCD59) to Identify Women with Gestational Diabetes Mellitus Based on the 75 g OGTT Using the WHO Criteria: A Prospective Study of Non-Diabetic Pregnant Women in Ireland. Bogdanet D, Toth Castillo M, Doheny H, Dervan L, Luque-Fernandez MA, Halperin JA, O'Shea PM, Dunne FP. J Clin Med. 2022 Jul 4;11(13):3895. doi: 10.3390/jcm11133895

Quality of patient-reported outcome reporting in trials of diabetes in pregnancy: A systematic review. Newman C, Kgosidialwa O, Dervan L, Bogdanet D, Egan AM, Biesty L, Devane D, **O'Shea PM**, Dunne FP. Diabetes Res Clin Pract. 2022 Jun;188:109879. doi: 10.1016/j.diabres.2022.109879. Epub 2022 Apr 25

Major disparities in patient-reported adherence compared to objective assessment of adherence using mass spectrometry: A prospective study in a tertiary -referral hypertension clinic.

Curneen JMG, Rabbitt L, Browne D, O'Donoghue DF, Alansari Y, Harhen B, Ní Ghríofa A, Ferguson J, McEvoy JW, Lappin D, Finn DP, **O'Shea PM**, Dennedy MC. Br J Clin Pharmacol. 2022 Feb 23. doi: 10.1111/bcp.15292. Online ahead of print

<u>A survey of practice in the management of haemolysis, icterus and lipaemia in blood specimens in the United Kingdom and Republic of Ireland.</u>

**Costelloe, Š.J, Rico Rios, N**, Goulding, N, Mistry, H, Stretton, A, De la Salle, B, Hepburn, S, Thomas, A, Atherton, J, Cornes, M. Annals of clinical biochemistry 2022, 59(4), 222–233. doi.org/10.1177/00045632211059755

Higher Inflammation Is Associated with Cardiometabolic Phenotype and Biochemical Health in Women with Obesity.

Killeen SL, Byrne DF, Geraghty AA, **Kilbane MT**, Twomey PJ, McKenna MJ, Yelverton CA, Saldova R, Van Sinderen D, Cotter PD, Murphy EF, McAuliffe FM.Ann Nutr Metab. 2022;78(3):177-182. doi: 10.1159/000522564. Epub 2022 Mar 18

#### No effect of maternal calcium intake and bone resorption during pregnancy on offspring bone mineral density at age 5 years.

Curtin L, Conway MC, **Kilbane MT**, McKenna MJ, McAuliffe FM. Osteoporos Int. 2022 May;33 (5):1165-1170. doi: 10.1007/s00198-021-06250-5. Epub 2021 Dec 1

Sweat testing in the modern era: A national survey of sweat testing practice in the Republic of Ireland. Maguire B, **Blake O**, Boran G, **Borovickova I**, Abdelfadil S, Murray C, Elnazir B, Linnane B. J Cyst Fibros. 2022 May;21(3):416-421. doi: 10.1016/ j.jcf.2021.09.012. Epub 2021 Oct 4

Reference intervals for commonly requested biochemical and haematological parameters in a healthy Irish adult Caucasian population. Islam MN, Griffin TP, Whiriskey R, Hamon S, Cleary B, **Blake L, Griffin DG**, Griffin MD, Krawczyk J, **O'Shea PM**. Ir J Med Sci. 2022 Feb;191 (1):301-311. doi: 10.1007/s11845-021-02535-0. Epub 2021 Feb 11

Association between vitamin D deficiency and the risk of prevalent type 2 diabetes and incident prediabetes: A prospective cohort study using data from The Irish Longitudinal Study on Ageing (TILDA). McCarthy K, Laird E, O'Halloran AM, Walsh C, Healy M, Fitzpatrick AL, Walsh JB, Hernández B, Fallon P, Molloy AM, Kenny RA. E Clinical Medicine. 2022 Sep 17;53:101654. doi: 10.1016/ j.eclinm.2022.101654. eCollection 2022 Nov

## Report on the 44 th Annual Conference of the Association of Clinical Biochemists in Ireland, 14-15 October, 2022

Compiled by Dr. Heloise Tarrant (St. Vincent's University Hospital, Dublin), Ciara Cunning (Mater Misericordiae University Hospital, Dublin), Ruth Cullen (Mater Misericordiae University Hospital, Dublin), Micheál Ryan (University Hospitals Limerick), Amy Gillick (CHI Temple Street, Dublin). Photography by Dr. Peadar McGing

The ACBI 44<sup>th</sup> Annual Conference was held in Cork on 14-15<sup>th</sup> October, 2022. The venue was the Kingsley Hotel, which has a strikingly lovely location on the banks of the River Lee and is within a short walk of the vibrant city centre.

The conference was opened by Dr. Seán Costello, Consultant Clinical Biochemist at CUH and the President's Address was delivered by Dr. Jennifer Brady, President of the ACBI and Consultant Clinical Biochemist at CHI. Dr. Brady extended a warm welcome to all the national and international speakers and delegates attending the conference. As the ACBI's first 'in-person' annual conference since 2019, this occasion afforded a very welcome opportunity to renew or make new professional links and friendships, face-to-face, after a turbulent 24 months which included great challenges arising from the COVID emergency and the HSE cyber-attack. Dr. Brady extended special welcome to the EFLM President Dr. Tomris Ozben, EFLM Member-at-Large Dr. Pilar Fernandez-Calle and to Dr. Deirdre O'Brien, National Clinical Lead for Pathology, thanking them for taking time from their very busy schedules to join the conference.

Dr. Pilar Fernandez-Calle took the floor giving a brief summary of the EFLM operational structure and membership; approximately half of IFCC members are represented by EFLM, including the ACBI. She explained that the operational structure of EFLM consists of an Executive Board and five Committees which carry out their tasks via Working Groups. The five Committees are Communications, Education & Training, Profession, Quality & Regulations, and Science. Membership of Committees and Working Groups is by application and open to nominations by national societies (the ACBI in Ireland) when a call for nominations is issued.

The first session of the conference was chaired by Dr. Paula O'Shea, Consultant Clinical Biochemist at MMUH. The session's focus was Rare Diseases, with three fascinating talks covering the carer's perspective, current Irish research on rare inherited disorders and, finally, establishing Rare Disease Care Pathways for the Irish healthcare system.

The first speaker, Ms. Anne Lawlor, gave the carer's perspective as mother of an adult child with 22q11 deletion syndrome (DiGeorge syndrome). Hearing the patient perspective is so important to us in laboratory medicine and was a fitting way to begin the conference. Ms. Lawlor is the founding member of 22q11 Ireland, a parent-led voluntary organisation advocating for and raising awareness of this complex

rare syndrome. She spoke of her daughter Áine, who is a member of the 22q11 YEEP (Young Expert by Experience Panel) group, which gives the lived experience so essential to developing supports and care pathways for people impacted by this condition.

The second speaker was Prof. Sally-Anne Lynch (UCD School of Medicine), a member of IRDiRC (International Rare Disease Research Consortium) taskforce on indigenous populations. Her research group has identified several rare disease genes which work has translated into effective genetic tests to aid clinical diagnosis. She spoke in particular of the work leading to their recently published catalogue of over 100 inherited rare disorders found amongst the Irish Traveller population and how it can be used to facilitate a targeted genetic approach to clinical diagnosis of rare diseases in this ethnic group.

The final speaker of the first session was Dr. Alana Ward (National Rare Diseases Office) who shared with us her work in designing rare disease care pathways for the Irish healthcare system. She reminded us that while rare diseases are individually of very low incidence, together they account for a very significant proportion of the hospital population, and that 4.2% of the Irish population have a rare disease diagnosis by age 17 years. Through this national initiative, optimal care pathways have been developed for 29 rare diseases. Furthermore, by identifying common patient needs and healthcare professional interventions across the different pathways a model template for a rare disease care pathway has also been developed. Implementation of these pathways is now a priority.

Dr Antoinette Tuthill, Consultant Endocrinologist of Cork University hospital, opened session 2 with an engaging talk on "What to expect when you're expecting....Menopause".

This talk covered the diagnosis and management of menopause. Dr. Tuthill outlined some of the challenges of perimenopause diagnosis and the multisystem symptoms of menopause. The talk also highlighted menopause associated biochemical alterations and development of metabolic syndromes including cardiovascular disease and type 2 diabetes.

Menopause symptoms may severely affect a woman's health and quality of life. Dr. Tuthill discussed recommended effective treatments to relieve menopause symptoms and emphasised that females who start Hormone Replacement Therapy (HRT) within 10 years of menopause derive cardiovascular protection. Dr. Tuthill drew upon the example of HRT use as the most effective therapy for osteoporosis prevention and vasomotor symptoms. The talk also pointed towards research based evidence of long term

risks associated with HRT and the importance of biochemical monitoring throughout therapy.

The talk progressed to testosterone replacement in menopause. The NICE Menopause Guideline (NG23) and the British Menopause Society recommend that a trial of conventional HRT is given before testosterone supplementation is considered and that testosterone replacement should only be considered in women who complain of low sexual desire after a biopsychosocial approach has excluded other causes. Baseline testosterone levels should be measured by liquid/gas chromatography. Levels should be reassessed 3 to 6 weeks after commencement. Oral oestrogens and conjugated oestrogens can reduce the effectiveness of testosterone treatment. It is important that monitoring of testosterone continues every 6-12 months to ensure that levels remain within the female physiological range in order to minimise adverse effects. Dr. Tuthill stressed that clinical assessment of potential adverse effects is equally important as some women are more sensitive to physiological levels of androgens.

In conclusion Dr. Tuthill re-emphasised how "The effects of menopause are often misunderstood and underestimated, that menopause can impact on health significantly in both the long term and short term". Despite this, many women are unaware of the effects and are confused about benefits and risks of treatment options. Guidelines like NG23, developed by leading experts in the field and based on comprehensive review of all existing evidence, provide healthcare professionals and with the necessary women information to empower them to make informed decisions about the choice of therapies available. It is imperative that all women have access to advice on how they can optimise their menopause transition and in the years beyond and there should be an individualised approach in assessing menopausal women, with particular reference to lifestyle advice, diet modification as well as discussion of the role of HRT.

Dr. Jennifer Brady, Consultant Clinical Bicohemist, Chrildren's Health Ireland (CHI), Temple Street followed with a talk on "Expanded neonatal screening - The Irish Experience". She outlined that screening is not just about the laboratory testing, but is an entire programme, all elements of which are monitored by key performance indicators.

Newborn blood spot screening was introduced in the Republic of Ireland in 1966 when screening of Phenylketonuria (PKU) commenced. The Irish programme has been tailored for the local population and the incidence of disorders occurring within the Irish population. A further 8 conditions have been added to the screening programme; Homocystinuria, Classical Galactosaemia, Maple Syrup Urine Disease, Congenital Hypothyroidism, Cystic Fibrosis, Glutaric Aciduria Type 1, Medium Chain Acyl Co A Dehydrogenase deficiency. May 2022 marked the most recent introduction of screening for an immunological disorder, adenosine deaminase deficient severe combined immunodeficiency (ADA-SCID). The Irish programme is co-ordinated by the National Newborn Bloodspot Screening Laboratory in CHI at Temple

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street on behalf of the Health Service Executive and the Directorate of Health and Wellbeing - Public Health and Child Health. It is a multi-stakeholder programme. Dr. Brady's talk summarised how the programme has been expanded in Ireland and reviewed how other programmes internationally have expanded where our EU counterparts go way beyond the listed nine disorder testing.

Newborn screening (heel prick testing, Guthrie testing) is a proven high value public health intervention which is unfortunately not available to all babies on the planet. The international Federation of Clinical Chemistry and the International Society of Neonatal Screening have established a Task Force (TS-NBS) to partner with healthcare professionals and the government to support the introduction of screening. To help identify partner regions and to get a current picture worldwide of newborn screening, а questionnaire has been developed. To stimulate equity in Europe a collaboration between the European Reference Networks (ERNs) (including MetabERN for RITA for immunodeficiencies, IMDs and autoinflammatory and autoimmune conditions), the International Society for Neonatal Screening (ISNS), the International Patient Organisation for Primary Immunodeficiencies (IPOPI), and the European Society for Immunodeficiencies (ESID-ISNS, IPOPI and ESID operating within the Screen4Rare initiative) has considered ten elements for effective operation of NBS programmes in Europe. These ten elements were listed in the talk.

The talk touched briefly on the laboratory aspects of expansion involving method verification and determination of cut off values. The latter requires analysis of a large number of 'non-affected' cards, verification of a preliminary cut off with known positive cases, review of other laboratory cut offs and literature, with consideration for gestational age and birth weight. Verification also requires analysis of normal cards to estimate false positive rate.

Dr. Brady emphasised that today we face enormous opportunities of expansion. These are partially driven by technology both for the analysis of markers and with new treatments. While newborn screening is accepted as beneficial to public health, it can cause harm (e.g. unnecessary concern in the presence of false positives, or by treating children with mild phenotypes).

Results of a national survey in May 2022 revealed that "86% of parents want to know if their newborn has a rare condition" and "65% of parents are in favour of screening newborns for as many conditions as possible". DNA based technology is also expanding and increasingly being used in newborn screening and we are aware that everybody is talking about whole genome sequencing. There have been very different responses to these expanding opportunities worldwide. In the UK there is the classic screening model of decision making. The US is focused on a more clinical model when contemplating expanding screening. Dr. Brady's talk proceeded to highlight the profound conflict over what criteria are relevant to adjudicate the inclusion of new tests in screening and what we should be doing in the face of what we can do.

The Department of Health is now progressing the

development of a methodology for prioritisation of proposed new conditions on the screening list. There will be a more extensive evidence assessment and evaluation by HIQA. Dr. Brady highlighted points from the HIQA 'review of processes in use to inform the expansion of newborn bloodspot screening programmes'. "There are important ethical, legal and social implications to be taken into account, which impact a range of stakeholders including, but not limited to, the child, family, and healthcare workers providing screening and follow-up services".

Closing remarks from Dr. Brady included emphasis on the enormous opportunities in terms of newborn screening expansion but limits have to be set. We need solid health technology assessment. We need some carefully reasoned exceptions and we need careful context for decision making. Newborn screening is positive but expansion "needs to be evidenced based and the benefits must outweigh the harm".

After a hearty lunch, we were heard a fantastic showcase of the excellent work being carried out by ACBI members. Oral presentations were selected from submitted clinical case and research abstracts. The case presentations included a case of Meropenum-induced hypertriglyceridaemia in an infant (Dr Pamela Chiwara), a case of reverse pseudohyperkalaemia in two patients with varying WBCs and H indices (Dr Lucille Kavanagh-Wright) and aberrant visual identification of icterus in a specimen from a patient with severe neutropenic sepsis on Eltrombopag therapy (Dr Briedgeen Kerr). The research presentations included an evaluation of capillary based sampling and laboratory measurement as a convenient adjunct primary care testing model for management of patients with chronic disease (A Kearney) and 'Calcium verification with a difference?' (Ayisha Azeez).

This was followed by an interaction section which has become a very popular element of the conference and certainly helps to keep attendees 'on their toes'. Ruth Cullen (Mater Misericordiae University Hospital, Dublin) delivered an excellent session which covered a range of dilemmas faced in the Biochemistry Laboratory and discussed available best practice guidance to help deal with such dilemmas. These included;

- Ammonia analysis and the guidance for laboratories to accept all blood samples for ammonia even if the quality of the sample has been compromised. [2018 MetBioNet Guideline for the Investigation of Hyperammonaemia]
- How laboratories deal with samples/tests which exceed defined Lipaemic/Haemolysis index cutoffs and measurement of HIL IQC in laboratories. We were reminded that a recent survey of practice in the management of haemolysis, icterus and lipaemia in blood specimens in the United Kingdom and Republic of Ireland (Costelloe et al. Annals of Clinical Biochemistry 2022, Vol 5 (4) 222-233) found that only 37% of respondents measured HIL IQC, with variable frequency.
- Testing strategies for thyroid dysfunction with reference to the NICE guideline (NG145) -

Thyroid disease – assessment and management.

- Minimum re-testing interval for Vitamin B12 as recommended in the UK National Minimum Retesting Intervals in Pathology Guideline [G147] (updated March 2021)
- Inclusion of non- HDL and TC:HDL ratio in the lipid profile provided by laboratories with reference to the 2019 ESC/EAS Guidelines for the management of dyslipidaemias and NICE Clinical Guideline 181.

After a short break, the opening talk of the Nutrition and Health session was titled "Vitamin D status in the Irish population - cause for concern, and if so, how to address?" by Prof Kevin Cashman, University College Cork. It was brought to our attention that in the fast moving field of vitamin D, approximately 15 papers are published per day, certainly making it difficult to keep up with! Prof Cashman reminded us of the important roles of vitamin D in calcium homeostasis, muscle and other non-skeletal roles - association studies suggest a link between vitamin D deficiency and cardiovascular diseases, diabetes, inflammatory, some infectious and immune disorders, certain cancers, and a higher mortality. The presentation highlighted the variability when defining vitamin D deficiency and the goal of the Vitamin D Standardization Program (VDSP) to standardise vitamin D analysis and minimise the impact of method related differences. Prof Cashman gave us valuable insight into vitamin D status in the Irish population with 12% of Irish adults and 21% of teenagers being vitamin D deficient (<30nmol/L). He stressed the lack of vitamin D intake in the Irish population in comparison to other European countries and how this micronutrient malnutrition in the public could be reduced by increasing diversity of food, supplementation and food fortification.

The second talk of the session was titled "Dietary Management of Epilepsy" by Dr Niamh McSweeney, Consultant Paediatric Neurologist at Cork University Hospital. Dr McSweeney reminded us that there are over 250 inborn errors of metabolism with epilepsy, a third of which are treatable and some of which respond well to the correction of the metabolic deficit. Epilepsy is known to affect 1-2% of the population and the presentation covered the many reasons that a seizure might occur including failure of brain metabolism, vitamin/cofactor deficiency, accumulation of toxins/ abnormal storage material. disruption of neurotransmitters or associated malformations of cortical development. Dr Sweeney presented several examples of inborn errors of metabolism amenable to targeted treatments, thus making metabolic epilepsy a good example of precision/personalised medicine.

Despite being the final presentation of the day, 'Obesity Disease Management including bariatric surgery and its biochemical implications" by Diarmuid Duggan was eye-opening and full of character keeping us all alert and interested. Mr Duggan, a dietician at the Bon Secours Hospital in Cork ("born in the Bons, work in the Bons and likely to die in the Bons") spoke of the complex nature of obesity disease and the need to facilitate individuals to meet their personal goals in a

non-judgemental person centred approach. Mr Duggan discussed the consequences of weight bias and the role of genetics, epigenetics and the environment in obesity disease. The presentation centred around obesity disease management (lifestyle medicine, medications, endoscopy and surgery) and covered the different surgeries available and the lifelong follow up required by these patients.

The second morning of the conference welcomed Professor Robert Flanagan, retired Consultant Clinical Scientist and Director of King's College Hospital NHS Foundation Trust's Toxicology unit. Professor Flanagan has authored in excess of 200 papers and 4 books, and is a Fellow of the Royal Society of Chemistry and of the Royal College of Pathologists, and an Honorary Fellow of the College of Mental "Laboratory Health Pharmacists. In his talk Investigations Post-mortem" Professor Flanagan provided a fascinating insight into how alongside available evidence, biochemical investigations aid post -mortem analysis. He described the complex collection and analysis of samples obtained from deceased patients, such as blood, hair and vitreous humour in post-mortem investigations and the subsequent challenges of sample degradation/contamination and interpretation without defined reference ranges and possible change in analyte behaviour after death. This talk drew from Professor Flanagan's illustrious career where he has worked alongside the legal system advising on toxicological issues and as consultant to the United Nations Office on Drugs and Crime. A topic not often explored by many of our members, it was an engrossing and enjoyable presentation.

Prof. Flanagan's talk was followed by a session on "International Developments in Laboratory Medicine". Ms. Ruth O'Kelly, former Principal Biochemist of the Coombe Women and Infants University Hospital and current INAB Technical Assessor opened the session. Her presentation entitled "New ISO15189 Standards -What you need to know" provided an intriguing insight into relevant changes following the upcoming revision to the standard that has been drafted to reflect the demands of the medical laboratory community. Risk management strategies and service agreement procedures are key-stone points of this revised edition. Provided samples can correctly be traceable to the patient, the processing of potentially compromised samples, or samples lacking the prescriptive identification requirements is revised in a clinical decision-making section which now provides greater consideration to the potential consequences of not processing such samples given the current rigidity to the service requirements. Ruth's talk reiterated how compliance to standards maintains laboratory service quality in a patient focused manner and provided a fantastic foresight before the eventual implementation of this updated standard to our medical laboratories.

Dr. Bernard Gouget, of the University Hospital in Paris Descartes, Counsellor for public health at the Fédération Hospitalière de France and Chair of the IFCC-CPD was next to present. In his fascinating talk "working in the Lab (from Home)", Dr. Gouget

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explored the rapid evolution of communications and computer technologies and with it the growing potential of the health care system to utilise this technological renaissance. The talk teased a futuristic, and almost surrealistic world where artificial intelligence and machine learning would be innovative to patient diagnosis, management, personalised medicine and clinical research. It was exciting to imagine the profound implications for biochemistry laboratories regarding sample processing, automation, decision limits, reference ranges, and the availability of patient data such anticipated advancements potentiate. Dr. Gouget also discussed advancements to the preanalytical phase including drone-delivered patient samples. It was exciting to discuss such vast scientific potential in its infancy and appreciate the opportunity for communication between laboratorians, clinicians and patients unlimited by distance.

The session was concluded by esteemed guest Dr. Pilar Fernandez Calle of the Dept. of Laboratory Medicine Hospital Universitario La Paz Madrid, Spain and EFLM Member-at-Large 2022-2023. Dr. Fernandez Calle's talk "Building a Biological Verification Database", drew from expertise gathered over a formidable career and discussed the challenges overcome, and the incredible work performed by an EFLM task-force in systematically reviewing within and between-subject biological variation data available on Westgard.com. This data is paramount to set analytical performance, in method specification, result/ IQC and EQA interpretation. Dr. Pilar Fernandez Calle explained the limitations that non-standardised, obsolete or direct methodologies have imposed on the integrity of certain biological variation data and the associated clinical consequences. She described how more robust data was generated from indirect methodologies in multicentre patient studies based on specific inclusion criteria, coefficient of variation, confidence intervals and reference change value. In a published Variation Data Critical Appraisal Checklist a specialised criteria for production of reliable and translatable biological variation was established. This engrossing presentation revisited and revitalised historical work imperative to the daily functioning of medical laboratories.

After an opportunity to review and appreciate the fantastic poster entries, the final session of the meeting commenced with Associate Professor of Pharmacy in Trinity College Dublin, Dr Tamasine Grimes delivering a talk on "hospital-based pharmacy". Dr. Grimes utilised examples to encapsulate a patient's pharmaceutical/therapeutic journey undertaken under the supervision of their clinician. She discussed challenges associated with drug cost and availability, reconstitution time/half-life and bioavailability as well schedule as treatment adherence. From this presentation arose the conversation about the importance of communication between not only patients and clinicians, but colleagues within the healthcare system and how inviting communication between healthcare disciplines like the biochemistry laboratory and the requesting clinicians potentiates enhancement of the overall patient focused healthcare

service.

The final speaker was Dr. Maria Donovan, Lecturer in Clinical Pharmacy with University College Cork. Dr. Donovan focused primarily on the aminoglycoside antibiotic gentamycin in her presentation "Unlocking the Potential of Therapeutic Drug Monitoring for Optimisation of Dosage Regimens". Gentamycin is a bactericidal commonly measured in the biochemistry laboratory and must be carefully monitored to ensure dosage remains within a carefully controlled target range that is cognisant of the status of kidney function. Dosage aims to rid the present infection whilst avoiding the unwanted sequelae of side effects including nephrotoxicity and deafness. Dr. Donovan discussed how through a specialised computer programme, a given dosage of gentamycin can be monitored in a virtual simulator to mimic its affect, breakdown, half-life and side effects in a simulated environment. This thought-provoking talk instigated conversations on the limits and potential of such technology to predict the journey and behaviour of other commonly monitored therapeutic drugs in the body.

The event concluded with conference organising



Dr. Jennifer Brady, President of the ACBI



Dr. Sean Costelloe, Chairman Conference Organising Committee

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committee chair Dr Seán Costelloe presenting the medals for best clinical case to Dr Briegeen Kerr (Cork University Hospital), best research presentation to Aisha Azeez (Mater Misericordiae University Hospital) and the Geraldine Roberts medal for best poster to Dr Jennifer Brady (Children's Health Ireland) for a poster presentation relating to AST Assay Interference due to Macro-AST.

The conference was highly enjoyable and the educational value was exceptional. The efforts of the conference organising committee at Cork University hospital, the ACBI and the event sponsors to make the meticulously planned event a reality for the first time since the COVID-19 pandemic was universally recognised and appreciated. The conference thus drew to a close after intriguing talks and knowledge presented and shared among our colleagues of multiple disciplines both nationally and internationally. Attendees not only enjoyed the expertise, but the much -missed company, networking opportunities, and conversation that only comes with in-person gatherings. The 44th Annual ACBI Conference was ultimately a huge success and the 45th conference is already greatly anticipated.



Dr. Niamh McSweeney (speaker), Professor Kevin Cashman (speaker), Diarmuid Duggan (speaker), Orla Maguire (Chair -Nutrition and Health Session)





Dr. Jennifer Brady, Ruth O'Kelly (speaker), Dr. Séan Costelloe, Dr. Pilar Fernandez-Calle (speaker) Prof. Tomris Ozben (EFLM Member-at Large), Dr. John O'Mullane (Chair - International Developments in Laboratory Medicine Session), Dr Bernard Gouget (Speaker)



Dr. Jennifer Brady (recipient of Geraldine Roberts Medal for best poster), Dr. Sean Costelloe, Briedgeen Kerr (recipient of best case presentation medal)



Professor Robert Flanagan (speaker)



The IEQAS (Irish External Quality Assessment Scheme) Annual Participants' Conference was held as a hybrid meeting on Thursday, 06 Oct 2022 at the very comfortable and by now also very familiar surroundings of the Ashling Hotel, Parkgate St, Dublin. I was lucky to win the in-person attendance registration as sponsored by the ACBI, and as I haven't attended a conference 'in real life' since before Covid hit, I was particularly happy to be able to attend on the day.

The IEQAS conference always promises a wide and varied programme and this year did not disappoint, with topics covering Lab Greening, paediatric hepatitis, the laboratory I.T. programme and CAR-T cell therapy heading up the morning's agenda. After a very enjoyable lunch and equally enjoyable opportunity to catch up with other colleagues, the afternoon workshop and case studies sessions began, covering the four main schemes served by IEQAS, namely Chemistry, Haematology, Microbiology and Transfusion. The meeting was warmly opened by Peadar, IEQAS Chair, who gave an interesting background summary of his own career in laboratory medicine (also beginning in 1981) and allied it with the inception and similarly successful development of IEQAS. Peadar stressed the importance of supporting local (yet another lesson learnt from Covid!) and highlighted the many benefits of IEQAS membership. He also stressed the importance of volunteering with regards to various IEQAS committee and specialist advisor roles, and put out a plea for anyone with an interest and/or expertise to approach IEQAS to volunteer for this work, which he has found especially enjoyable and educational.

While I enjoyed all aspects of the material covered on the day, I will openly admit that the main topic of interest for me on the day was the subject of 'The Rise of Lab Greening' delivered by the very impressive Dr Una FitzGerald, who is for all intents and purposes the European pioneer for same.

Having volunteered to be one of the ACBI green labs representatives I have seen Dr FitzGerald's name cropping up repeatedly during my research so it was a treat to hear her speak in person. Dr FitzGerald's laboratory at CÚRAM (the SFI Research Centre for Medical Devices based at University of Galway) became the first in Europe to be awarded Green Lab Certification. She traced her interest back to the rather random purchase in 2018 of a book named 'No more plastic' by Martin Dorey (ISBN 1785039873). This book led her to a personal epiphany on the impact that all of us have on the planet and how we can not only reduce our environmental impact, but also how our small actions, both at home and at work, can add up to a big difference. Many of us enjoy books and are occasionally moved by them, but Dr FitzGerald went many steps forward and took the ethos of this book i.e. 'together we can fix this' and applied it, with the guidance from the 'My Green Lab' (MGL) organisation, to make significant changes to how she and her laboratory colleagues carry out their daily work.

As she stated, there are always good reasons that can be found for not making 'climate friendly' changes to our lives, and the Covid pandemic and the war in Ukraine are often cited as reasons to postpone dealing with the 'wicked problem' of the climate crisis for a later, unspecified time. Dr FitzGerald however is not one for excuses and encourages a more positive, proactive approach. She recommended another book 'What If Solving The Climate Crisis Is Simple?' by Tom Bowman (ISBN 1789047471) which provides more food for thought with the statement 'make every decision a green decision', an approach that can be used in all aspects of life and work.

These green behaviours involve focusing on the four pillars of Water, Energy, Chemistry and Waste. These pillars form the scope of the Irish Green Labs climate action (https:// irishgreenlabs.org/), a group established in July 2021 from the SEAI's Working Group for Public Sector Labs. This group aims to assist public sector labs to optimise their energy management systems and to design targeted actions to combat any negative impact that laboratory activities could have on the environment.

Dr FitzGerald also gave us a whistle-stop tour of the origins of the sustainability in laboratories movement from its inception in the US, including the setup of ISL (International Institute for Sustainable Laboratories, link <u>here</u>) and My Green Lab (MGL), to The Sustainability Laboratory (S-Lab) and S.O.S. (Students Organising for Sustainability)in the UK, LEAF (short for the Laboratory Efficiency Assessment Framework) and the more recent initiation of the Irish Green Labs collective.

The resource that Dr FitzGerald mentioned that I was most familiar with was that of the Green Lab Certification program from MGL, which has been selected as a key indicator of progress for the UNFCCC High Level Climate Champions' 2030 Breakthroughs campaign. In the lead up to the COP26 Climate Change Conference, the MGL program had been chosen as a key player to help pharmaceutical and medical tech companies achieve the goal of a zero carbon world by 2050. It is of course also the perfect resource for clinical and research laboratories to inform their lab greening actions and goals. Having recently completed the My Green Lab Ambassador training (consisting of Smart Science Training Videos and Ambassador Assessment) I would encourage anyone else with an interest in the topic to take the time to check out this free and informative resource.

As the saying goes 'every journey begins with a single step' and hearing how far Dr. FitzGerald and many other labs have managed to come in the past few years was very impressive. I am glad and encouraged that this topic is becoming a more regular feature in meetings such as IEQAS and I hope to see the awareness and importance of the Green movement continue to go grow in relation to clinical laboratories in Ireland.

### Photos from the IEQAS Conference



Dr. Cillian O'Maoldomhnaigh (speaker), Dr. Peadar McGing (IEQAS Chairman), Dr. Una Fitzgerald (speaker)



Mr. Thomas Walsh (speaker), Professor Larry Bacon (speaker)





ACBI and ACB (Republic of Ireland Region)

## Upcoming Meetings and Courses



ACB (Republic of Ireland). Virtual Meeting. 7th February 2023. Abstract submission open. Closing date 5pm Friday 20th Jan. €100 prize for best abstract (open to all ACB members excluding consultants). Find out more <u>here</u>.

ECE 2023: 25th European Congress of Endocrinology, 13th-16th May 2023, Istanbul, Turkey. See <u>ECE 2023 | ESE (ese-hormones.org)</u> for general information and <u>Programme | ESE (esehormones.org)</u> for an update on symposia/lectures etc.

30th European Congress on Obesity. 17th-20th May 2023, Convention Centre, Dublin, Ireland. See <u>30th European Congress on Obesity (eco2023.org)</u> for general information and links to programme information.

50th European Calcified Tissue Society (ECTS) Congress. 15th-18th April 2023, Liverpool, UK. Details found at <u>Home - ECTS 2023</u>. See Scientific Programme at <u>https://www.ects2023.org/</u> <u>programme/</u>

Federation of European Biochemical Societies [FEBS]: <u>The 47th FEBS Congress. 8th-12th July</u> <u>2023</u>, Tours, France. Programme overview <u>here</u>.

Systematic review skills <u>course</u>. Ashling Hotel Dublin June 13th 2023. Numbers limited to 30. Fee: Students €50 (7 places left at time of writing); General €100 (11 places left at time of writing). Registration closes June 7th, 2023.

## Webinars/Guidelines/Editorials

European Federation of the Associations of Dieticians (EFAD) webinar—**The latest dietary guidelines on obesity and diabetes management**. Find <u>here</u>. 3 lectures, quite detailed, good slides. Posted early December 2022. 90 minutes. Some other interesting webinars on the webpage also.

It Ain't Over Till It's Over . . . but It's Never Over — Emerging and Reemerging Infectious Diseases. A reflective article in NEJM December 2022 (and a warning about not letting our guard down again) from Dr. Anthony Fauci who was an ever present face in the media during the Covid crisis. He is retiring from the National Institute of Allergy and Infectious Diseases in the US.

A complete guide to human microbiomes: Body niches, transmission, development, dysbiosis, and restoration. Everything you want to know (or don't) about our cohabiting microbiome, where they hide out and their benefits or otherwise to our health. A PDF version can be downloaded from the site.

Focussing on the gut microbiome a <u>review</u> cowritten by University of Alberta and University of Cork researchers concludes that the microbiome should not be ignored when addressing dietary guidelines and advice.

Guidelines from NICE on Type 2 Diabetes in adults: Management (updated in June 2022). PDF <u>here</u>.

Editorial on 'Success in Harmonization of Laboratory Measurements, <u>Yet More to Be Done</u>' (Journal of Applied Laboratory Medicine, November 2022).The ongoing quest to achieve harmonisation of lab generated results.

## Call for Nominations

Nominations are now open for ACB Republic of Ireland Regional Committee Chair, Secretary, Treasurer and Ordinary Member. Contact <u>karenheverin@beaumont.ie</u> for more information. Closing date Friday 13th January 2023.

### International Federation of Clinical Chemistry (IFCC) and European Federation of Laboratory Medicine (EFLM) Update Compiled by Alison Bransfield

There are a number of EFLM committee opportunities open at the moment. Please see <u>www.eflm.eu</u> for information on same:

 WG Promotion & Publications (WG-PP) (1 full member) closes on 15/Jan/2023

#### **IFCC WG vacancies**

- IFCC SD\_C-RIDL Committee on Reference Intervals and Decision Limits (1 member) closes on 06/Jan/2023
- IFCC CPD C-PR CPD Committee on Public Relations (1 member) closes on 31/Dec/2022
- IFCC EMD C-POCT (2 members) closes on 20/Jan/2023
- IFCC EMD C-KD (2 members) closes on 15/Jan/2023
- Under the auspices of the EFLM the Innovate Health Initiative (IHI) has launched a call for proposals under a number of different topics. The website is accessible <u>here</u>
- The EFLM has opened applications for the EFLM Scientific Research Grant 2023, details are available <u>here</u>
- Nominations have opened for the EFLM Academy available, see <u>here</u> for details
- Nominations have opened for the EFLM Academy Award, details are available <u>here</u>
- EFLM bursaries to attend EuroMedLab Rome 2023 are available, see <u>here</u> for details (additional bursaries are available for young scientists here)

Please note that applications are to be made through the ACBI council. If you are interested in volunteering for a committee position please contact the ACBI President, Dr Jennifer Brady

#### CCLM

 There is a new issue of 'Clinical Chemistry and Laboratory Medicine (CCLM)' available online from De Gruyter Online: Volume 61, Issue 2. This can be accessed through your EFLM Academy logon

#### **IFCC/EFLM News**

- The current issue of "EuroLabNews", the bi-monthly EFLM newsletter, is available online: <u>2022-Nov-Dec-</u> <u>EuroLabNews (eflm.eu)</u>
- The EFLM Task-Force Green Labs has developed the 2EFLM Guidelines for Green and Sustainable Medical Laboratories" which can be accessed <u>here</u>

#### **EFLM Academy:**

 All ACBI members should now have received their EFLM Academy login details. If you have not yet received yours please contact <u>secretary@acbi.ie</u>

- Please note that EFLM Academy membership includes access to CLSI documents
- The new EFLM e-learning academy has now launched and is a comprehensive educational resource
- The current issue of "IFCCNews", is available online: <u>IFCCeNewsDecember2022</u>
- The current issue of "eJIFCC", Volume 33-no4 is available online: <u>eJIFCC2022Vol33No4</u>

#### **Upcoming Meetings/Events**

#### EFLM

- EFLM has established a series of webinars covering different diseases and their diagnoses using biommarkers. The leaflet is available here: <u>https://www.eflm.eu/upload/ docs/Leaflet-lessons-in-immunochemistry.pdf</u>
- EFLM live webinars are available here: <u>https://www.eflm-elearning.eu/site/live-webinar</u>
- Previous webinars available at <u>https://www.eflm-elearning.eu/site/on-demand-webinar</u>
- AACC Learning Lab is now available free of charge for details see <u>https://area9lyceum.com/laboratorymedicine/</u>
- EFLM has established the Task-Force "Green Labs". For more information click <u>here</u>
- The EFLM Task-Group on Chronic Kidney Disease has published a position statement on the use of the race-free CKD-EPI equation. It may be accessed <u>here</u>
- XXV IFCC-EFLM WORLDLAB EUROMEDLAB ROMA 2023 May 21<sup>st</sup> – May 25<sup>th</sup> 2023. Early bird registration closes on 31/Mar/2023: <u>https://2023roma.org/</u>

#### Webinars

- IFCC is looking for volunteers to present webinars; contact ACBI president for information if interested
- EFLM Green Labs presentations are available and will be uploaded to the new ACBI website

#### Meetings

XXV IFCC WORLDLAB Roma May 21-25, 2023 http://2023roma.org

The IFCC General Conference 2022 presentations are available  $\underline{here}$ 

#### **IFCC/EFLM** websites

http://www.ifcc.org/ https://www.eflm.eu/

## Standardisation of COVID -19 serological assays: the provision of a common language

Dr. Marie Eagleton, Senior Clinical Biochemist, HSE National Drug Treatment Centre, Dublin



Abdi Ghaffari, Robyn Meurant, and Ali Ardakani, CC BY 4.0, via Wikimedia Commons

If you have a spare hour, attending the webinar 'Standardization of COVID 19 serological assays: Establishment of the WHO international standard and its importance' is worthwhile<sup>1</sup>. The webinar is presented by Dr Giada Mattiuzzo, Senior Scientist at the UK National Institute for Biological Standards and Control (NIBSC), which is the centre of the UK medical healthcare regulatory authority-MHRA. This institute supplies over 90% of WHO international standards.

Dr Mattiuzzo outlines the history, value and general processes used to generate reference biological materials. Biological reference standards enable the comparison and monitoring of assays/vaccines over time, operator, laboratory and even methods. A hierarchy of biological materials characterised by increasing uncertainty of measurement (UoM) and decreasing traceability is described. At the apex of the hierarchy is the primary reference material which has a zero UoM and high traceability. Patient samples whose potency is described relative to an internal assay standard, have the lowest traceability and highest UoM. When testing patient samples in an immunoassay, the potency of the samples are expressed relative to an internal assay control or calibrant, which itself should be calibrated against the WHO primary reference control. WHO international standards are the highest order of material for calibration of international standards worldwide and their potency is expressed in international units per ml (IU/ ml.) External controls that are used to assess the performance of an assay over time and with different operators and internal controls, have an intermediate UoM and traceability.

The conversion factor between IU/ml and a quantifiable mass such as ug/ml is often queried. However-IU does not refer to mass of a substance but to its potency or biological activity. Assay results expressed in international units, allow for comparison of sample results generated in different laboratories by a variety of methods, and the results are comparable between laboratories and over time - thereby providing a common language for comparative purposes. The use of this common language has proved to be valuable for establishing protective levels following vaccination, assessing vaccination status and in molecular diagnostics for identifying potency of viral load.

Dr Mattiuzzo outlined the process used to develop an international standard as described in WHO guidance document '*Recommendations for the preparation characterization and establishment of international and other biological reference* standards (2004) <u>https://www.who.int/publications/m/item/annex2-trs932</u>.

The approach has been used to identify and generate reference assay material for Lassa virus, MERS, and SARS CoV-2. The process commences by identifying the need to develop a standard. Sourcing the bulk material is the critical step in the process, particularly when dealing with emerging viruses. Once the material is sourced, it is characterised and formulated and then subject to product assessment which is usually done by 15 to 20 laboratories worldwide. Post assessment, the material is arbitrarily assigned an international unit value. This assigned value is close to the numerical value obtained by the majority of the assessing laboratories, even if these assays use different analytical techniques and express their results in different units. Once the material is assessed it is subject to stability testing using temperature acceleration studies; the aim is to have a shelf life between five and 10 years. At the end of this process statistical analysis is performed, an evaluation report is generated and submitted to the WHO Expert Committee on Biological Standardization and is available for public consultation. Following this, the decision is made whether or not to adopt the standard and if successful the standard is added to the WHO catalogue. The process from identification of the need for a standard, to standard availability for use, usually takes between two to three years.

Dr Mattiuzzo outlined the specific procedures and time line when generating the first WHO serological standard for SARS CoV2 (COVID-19). The virus, first isolated in January 2020, was followed by the WHO declaration of a global health emer-

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gency at the end of Jan 2020. Within two months, a research reagent for nucleic acid amplification was developed, followed by a reference panel of high, medium and low titre convalescent plasma for COVID 19. This intermediate panel was established within 3 months and was used as a bridge until the WHO standard panel was established. The research reagents were then calibrated to the newly characterised WHO international standard for retrospective reporting of results. Despite controlled sales, the stocks of international standards were depleted by August 2021. They have been replaced in the interim with secondary standards and the aim is to have a second primary standard available in the last guarter of 2022.

The candidate COVID-19 serological standard along with an eight member panel that included convalescent plasma samples from various sources, was evaluated by the 44 participating centres from 15 countries. All convalescent donors provided written consent and tested negative for the usual range of viruses (HIV, Hep B etc). The participating laboratories included vaccine developers, academic laboratories, commercial kit manufacturers and national control laboratories. One hundred and twenty five test methods were used to evaluate the standard, including 27 neutralisation assays, with both live and pseudotype viruses, seventy eight ELISA assays, including IgG and IgM and to both receptors binding domain and spike protein epitopes. Other assay methods included flow cytometry, lateral flow immunoassay and ACE 2 binding inhibitory assays. The candidate international standard, generated from a pool of 11 UK donors, resulted in the production of 3,250 ampoules, each containing 0.25ml of lyophilised material. The stability of the material as assessed by temperature acceleration studies using an in house ELISA against S1 subunit, estimated a loss of potency of 0.255% per year when stored at -20°C.

The value of expressing COVID -19 serological assay results relative to an international reference standard was discussed. Convalescent sera analysed in participating laboratories using a virus neutralisation assay and expressed as a 50% neutralisation titre demonstrated a much wider spread of results by comparison to expressing the results in relation to the reference standard in IU/ml. Use of the reference standard enables harmonising of results thereby enabling easy comparison of data. Such reduction in spread of results from different laboratories was also demonstrated for four spike protein antibody binding ELISA assays, each assay expressing results in different units: signal to cut-off, dilution factor, ug/ml and arbitrary units per ml. Prior to translating the result from each assay type into IU/ml the data was very difficult to compare. The value of expressing results in IU was also illustrated when doing a correlative study between two assays. Comparing 2 assays which expressed results in different units showed lower correlation that when both assays results were expressed as IU/ml.

The primary WHO serological standard for SARS CoV2 (catalogue no 20/136) was released in Dec 2020. The literature suggests that assay manufacturers either used the standard to calibrate their internal assay control or used it to generate a conversion factor to convert assay results to IU. There is also literature indicating that the standard was used to correlate vaccine efficacy with antibody titre. However there is evidence of misuse of the standard. Dr Mattiuzzo emphasised that the intended use of the standard is as a calibrant and that it should not be used as a validation tool, an internal control or for routine work. Validation panels can be sourced for such work and assays should be qualified using external quality assurance schemes. Sharing of reagents and procedures between laboratories can help standardise assays.

In the concluding part of the talk Dr. Mattiuzzo discussed the impact of new variants and variants of concern (VOC) on therapeutic responses and the requirement for reference materials which will enable assessment of responses to new variants. As the pandemic evolves new standards will be generated and ideally standards should have activity against all VOC. The need for higher titre standards has been identified particularly by assay manufacturers. Convalescent sera from individuals that have been vaccinated and have been subsequently infected tend have higher antibody responses that that observed with the first international standard, but continuity with the first standard is important.

Attending this webinar will make you aware of the true value and positive impact of international standards and also of the importance and benefits of international scientific collaboration in providing standardised materials.

https://www.aacc.org/education/all-webinars/webinars/2021/december/standardization-of-covid-19-serological-assays
Webinar courtesy of AACC, free registration courtesy of Ortho Clinical Diagnostics until 31 Dec, 2022.

## Meet your Council

#### President — Dr. Jennifer Brady.



Dr Jennifer Brady is a Consultant Clinical Biochemist at Children's Health Ireland since 2019. She graduated from UCD with an honours degree in Biochemistry. She then undertook a 'grade A' training programme in Clinical Biochemistry based in Cardiff, Wales, incorporating an MSc in Clinical Biochemistry and Molecular Biology at the University of Surrey. She undertook her PhD at Cardiff University before returning to Ireland in 2004 to take up posts as a Senior Clinical Biochemist in St Vincent's hospital and later a Principal Biochemist at the Mater Misericordiae University Hospital, Dublin. Jennifer obtained fellowship of the Royal College of Pathologists in 2011 and is on the European register for Specialists in Laboratory Medicine. She has represented the ACBI at many forums including IEQAS, National Paediatric Diabetes Audit Feasibility Steering Committee, and at European level on the EFLM working group 'Register'. She has been chair of the ACB Republic of Ireland region since 2020.

Jennifer has been involved in the teaching and further education of clinical biochemists, undertaking the role of ACBI tutor from 2012 -14 and again from 2016-2018. She also lectures on the UCD MSc in Clinical and Diagnostic Biochemistry. She was appointed an Associate Clinical Professor at UCD School of Medicine in 2021. She maintains an active interest in research with a number of peer reviewed publications, and supervises projects for MSc students.

#### Vice-President — Dr. Seán Costelloe.



Dr Seán Costelloe is a Consultant Clinical Biochemist and Head of Department at the Department of Clinical Biochemistry, Cork University Hospital since 2017. He studied for a BA(Mod) in Natural Sciences (Biochemistry) at Trinity College Dublin, before taking on PhD and MSc studies at University College London. From 2007, Seán spent time as a Trainee and Senior Biochemist at the Royal Free Hospital in London, before taking on a Principal position at Leeds Teaching Hospitals NHS Trust, and a Consultant position at University Hospitals Plymouth NHS Trust.

Seán is a fellow of the Royal College of Pathologists and is on the European register for Specialists in Laboratory Medicine. He sits on the Irish Gestational Trophoblastic Disease Guideline and Steering Groups and is currently involved in the Working Group to inform the strategic direction of laboratory medicine. Internationally, Seán is a member of the ACB Special Interest Group for the Preanalytical Phase and the EFLM Preanalytical Working Group, as well as the European Society for Emergency Medicine Blood Sample Guideline Working Group.

He is the current Vice President of the ACBI and past President.

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#### **Clinical Biochemistry News**

#### Secretary - Dr. Peadar McGing.



Dr. Peadar McGing is the current Secretary of ACBI, assistant editor of the ACBI/ACB Rol newsletter, and also current Chair of IEQAS. Fadó, fadó, he graduated from UCC with a BSc, adding a PhD and an MSc (Clinical Biochemistry) from TCD, and finally FRCPath. He is also on the European register for Specialists in Laboratory Medicine (EuSpLM).

Having worked in the Mater Hospital for almost four decades he retired (kindof) as a Principal Clinical Biochemist late in 2020. Peadar's special interests are in education, fluid biochemistry, tumour markers, and history of laboratory medicine. In 2022 he was awarded Fellowship of the ACB, an award 'created to recognize individuals who have made an outstanding contribution to the practice of clinical biochemistry and laboratory medicine'.

Away from Clinical Chemistry Peadar is an enthusiastic participant in athletics and competes in a wide variety of track and field events.

#### Treasurer — Karen Heverin.



Karen Heverin is a Senior Biochemist at Beaumont Hospital in Dublin. She was awarded a B.A. Mod Hons Biochemistry at the University of Dublin, Trinity College in 2014 and took up her first position as a biochemist at the Mater Misericordiae University Hospital in 2015. Karen undertook a pilot training position which included secondments to various laboratories both in Ireland and further afield such as Cytogenetics, training at Queen Elizabeth University Hospital, Glasgow and Sanger/NGS experience at Health in Code, in A Coruna, Spain. She was awarded MSc Blood Sciences (Biochemistry) at the University of Manchester in 2019. Karen was appointed to a promotional role of Senior Biochemist at Beaumont Hospital in 2019, where she is currently based. Karen undertook the role of Secretary/Treasurer of ACB Republic of Ireland region in 2020. More recently, Karen successfully completed Part 1 of FRCPath examinations in Autumn 2021 and is currently working towards Part 2 examinations. Karen has also been appointed to represent the ACBI as a corresponding member of the IFCC Task Force for Young Scientists (TF-YS).

#### Council Member — Dr. Graham Lee.



Dr Graham Lee is Consultant Clinical Biochemist at the Mater Misericordiae University Hospital (MMUH) Dublin, Midlands Hospital Mullingar and National Orthopaedic Hospital Cappagh. He trained and worked in the UK where he attained Fellowship of the Royal College of Pathologists before taking up employment as a clinical biochemist (senior). He is Associate Professor at UCD where he is course director of the MSc in Clinical and Diagnostic Biochemistry and coordinator of several course modules. He is Past-President of the Association of Clinical Biochemists in Ireland and previous Chair of the ACB's Republic of Ireland (ROI) region as well as ACB ROI regional tutor. He is a European Specialist in Laboratory Medicine (EuSpLM) and contributes to the work of the European Federation of Laboratory Medicine as corresponding member of the Task Group for the EFLM's Postgraduate Syllabus Course and coordinator of the course's Liver module. He has worked on several Irish national programmes including the National Clinical Programme for Cancer and the National Clinical Programme for Pathology.

#### Council Member — Dr. Paula O'Shea.



Dr Paula O'Shea is a Consultant Clinical Biochemist & adjunct Clinical Lecturer/Assistant Professor at UCD School of Medicine. She is currently based at the Mater Misericordiae University Hospital & Our Lady's Hospital Navan. She has over 30 years' experience in clinical laboratory science, service development and research. She holds a Doctor of Philosophy (PhD) in Clinical Medicine, and Master (MSc) in Clinical Biochemistry, awarded by Trinity College Dublin (TCD). She is a Fellow of the Royal College of Pathologists (FRCPath), UK and is European Specialist in Clinical Chemistry and Laboratory Medicine (EuSpLM) registered.

#### Council Member — Micheál Ryan.



Micheál Ryan is currently employed as a Senior Clinical Biochemist in the Biochemistry Dept., University Hospital Limerick. Micheál graduated from the University of Limerick with a BSc. in Industrial Biochemistry (2003) and completed a MSc. in Biomedical Science (2007), University of Ulster, Coleraine.

He returned to the University of Limerick and completed a Post-Graduate Diploma in Quality Management – Lean Health Systems (2009). He successfully completed Part 1 of the FRCPath examinations in Autumn 2019.

Micheál formerly served as Trainee Representative for the ACB Rol Region (2017-2020).