LabMed Southern Region and UK NEQAS Clinical Chemistry meeting to celebrate the career of Les Perry: Immunoassay Past, Present and Future

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Following in the footsteps of the London Marathon, friends and colleagues old and new descended on London on Monday 22nd April 2024 for the LabMed Southern Region meeting which was jointly organised with UK NEQAS Clinical Chemistry to celebrate the career of Dr Les Perry, Consultant Clinical Scientist, South West London Pathology. Les has been a strong supporter of UK NEQAS over the years and has chaired our Immunoassay Specialist Advisory Group for a very long time! Laboratory Medicine should be indebted to him for his ideas and knowledge that have guided the EQA Schemes over the last decade or so.

Speakers of the day: (Back Row R to L: Gwen Wark, David Halsall, Brian Keevil, Cathie Sturgeon, Finlay MacKenzie, Bill Fraser. Front: Les Perry

The programme was organised to be themed on topics that Les is passionate about, namely endocrinology and training/supporting trainees. We were honoured that many of the great-and-good turned out to support this meeting and I am sure everyone in the audience realised that they were in for a treat! The meeting itself was not just a celebration but contained example after example of really sound, solid, science which emphasised the strength of the pioneering work that came out of the UK leading and pioneering immunoassay and endocrinology.

How EQA Leads and Supports Clinical Practice in Immunoassay and Endocrinology

The meeting opened with a double act of Dr Cathie Sturgeon and Finlay MacKenzie, both representing UK NEQAS Clinical Chemistry and having over 70 years of EQA knowledge between them. They talked about how EQA leads and supports clinical practice in Immunoassay and Endocrinology. Hopefully by now most laboratories are aware that EQA is much more than showing how you compare to your method group peers and ticking that box for UKAS and ISO 15189 accreditation. Cathie highlighted the importance of EQA in contributing to the clinical governance of laboratories and how UK NEQAS Schemes are able to respond to trends in laboratory provision with the development of new schemes and promoting awareness of clinical relevant interferences. Cathie gave a number of examples of her favourite analytes (which seemed to be all of them!) and how there has been a stimulus and the approach that has been taken to attain standardisation of analytes for which poor method agreement could compromise clinical care. I am sure we will all be pleased to hear that a Reference Method procedure for PTH is close to being available. Finlay took us back in history and showed us how EQA has developed over the years and how this has impacted the assays that are available on the market and practices within the laboratory. Once again a number of important examples were shown and it was probably a poignant reminder that some of the specificity issues of assays have been present for decades and though it may not now be a hot topic of discussion it really is important that these messages are communicated to laboratory personnel and service users as they usually explain a lot of anomalies. He inc1luded many recent examples to emphasise that EQA is still making a valuable contribution to identifying problems with assays to this day.

Mass Spectrometry Replacing Immunoassay — the not so new kid on the block that hasn t really taken off — pitfalls and challenges

Twenty years or so ago Mass Spectrometry was going to be the technology that addressed all the specificity failures of immunoassay and provide us with highly accurate results which could be relied upon … what happened? Professor Brian Keevil, Consultant Clinical Scientist from Manchester University Hospitals NHS Foundation Trust showed that despite the analytical superiority of Mass Spectrometry, the variation on EQA is much wider between users when compared to some immunoassays. This observation is supported by other projects, one being the HarmoSter Project which reviewed steroid analysis across ten European laboratories. The main reason for this is due to the variation in sample preparation, calibration and columns and methodology used in our LC-MS/MS systems. There has also been a lack of uptake of Mass Spectrometry. The most obvious reason being the expense of the equipment, lack of automation and also the requirement for highly trained staff to consistently operate such systems. Brian concluded that LC-MS/MS will never replace immunoassay but it does plug many gaps that immunoassay cannot cover or is deficient at and it offers big improvements in the quality of measurement. With careful implementation LC-MS/MS can successfully be used in a routine laboratory and the future way forward for LC-MS/MS should be as a translational tool to bring newer more relevant methods into clinical use.

Trials, Tribulations and Triumphs of Vitamin D and PTH Assays

Professor Bill Fraser took the session before lunch and took no prisoners in his honest and factual account of the development of PTH and Vitamin D assays. Bill walked us through the story of PTH starting back in the 1850s when Sir Richard Owen dissected a Rhinoceros from London Zoo. Sir Owen was first to identify the parathyroid gland. Medical and scientific developments over the years led Berson and Yalow to recognise multiple circulating forms of PTH using RIA in 1968. The Nobel Prize in 1977 went to Yalow for the development of RIA, though it could be argued that the UK's own Roger Ekins who had developed the mathematics of the models should have been included in this accolade. These multiple circulating forms of PTH have led to differences in PTH assay design which is why this assay is in such desperate need of standardisation. Bill explained the development of immunoassays and it may have been a surprise to some in the audience that laboratories used to develop their own antibodies with rabbits/hamsters in the laboratory. These antibodies would then go into laboratory made reagents which would then be shared with neighbouring laboratories. Obviously there was a problem when the rabbit/hamster died, but this process was in use for a number of years, well before the global giants started mass manufacturing the reagents as we know them today. Back in the day scientists in the laboratory would have been very hand s on as assays were in-house and it took considerably longer to get a single result! The knowledge and skills required for these assays have gone a long way to help us troubleshoot current assay problems. Bill finished his talk by showing some of the real limitations of current Vitamin D immunoassays. Though it might be a lot easier and quicker to use an immunoassay, you may not always get the correct answer!

Interactive Cases: Insulin and C-Peptide

Following lunch Dr Gwen Wark, UK NEQAS Scheme Organiser for Guildford Peptides kept us all awake with an interactive cases session. Gwen went in depth through three different hypoglycaemia cases with questions along the way. She showed that the glucose concentration impacts the interpretation of insulin and how you really need to understand how your assay reacts with different insulin preparations in order to correctly interpret insulin results. Sometimes you really do need to think like a detective and think outside of the box for an explanation of the results in front of you. This was the case for a patient who had injected themselves with animal insulin. Remember animals can be on insulin too and these preparations are different to the wide range of preparations used in humans. I am sure everyone in the audience learnt something which they could take back to their own laboratory!

Unusual TFTs

Thyroid testing started in 1958 and thyroid function testing is now one of the most frequently requested tests in the laboratory. As Dr David Halsall, who presented this session said, "Have we become factories which produce borderline abnormal thyroid results in patients who will not benefit from thyroid medication?" However, it is hard to imagine investigating thyroid disease without access to thyroid assays. Also, using EQA data David showed that there is clear blue water between the results of two of the main manufacturers for both TSH and fT4, and there are also differences in reference ranges also both within and between manufacturers. None of this does the profession any favours when clinicians are trying to interpret their results. David is also the LabMed representative on the IFCC Committee on Standardisation of Thyroid Function Tests and he reported back the progress on re-standardisation of fT4 assays which will see a significant increase to the numbers that we are used to now. David finished the session by going through four cases of a raised fT4 which when the sample was analysed on a different analyser gave very different fT4 results. Each had a different source of the reason why there was assay interference, but this served as a reminder to laboratories that assay interference in immunoassays is real, not just something you learn for exams, and if another laboratory asks you to analyse a sample, then please do!

How endocrine analytical testing has changed over time

The final session of the day was led by Dr Les Perry and he gave us some understanding of how we have got to where we are today in the field of immunoassay. The earliest bioassay known from Egyptian times was a pregnancy test which required women to urinate on barley and wheat seeds if they thought they were pregnant. If the barley/wheat germinated the woman was pregnant. We have come a long way since those early days with a lot of the early work with animal based antibodies which have now been superseded by monoclonal antibodies. As had previously been shown routine clinical laboratories were heavily involved in the design and development of immunoassays, including all reagent preparation. Several milestones since then have led to the proliferation of modern immunoassays which are now highly automated.

Les Perry showing a timeline of endocrine analytical testing

Les had a word of warning for laboratories in the future — robotics and Artificial Intelligence are on their way so scientists need to remain critical, ask questions and challenge the status quo. Get out of the laboratory and see patients and clinicians. You can help them both!

Together, everyone thanked Les for his support, advice and enthusiasm over the years. We hope to continue to benefit from this and wish Les Perry a long and happy retirement!

Mezzanine area with delegates networking over a tea break at Royal College of Pathologists, 6 Alie Street