In this issue
New Editor for Annals
Edmund and Jonathan Bow Out
From Chaos to Harmony Takes Time
British Biochemists Win Open Chemistry of Life in Sheffield
iCHROMA™

The simple dependable i-CHROMA™ CRP assay provides results:
- comparable to laboratory methods
- on a drop of blood
- within 3 minutes

Performance Characteristics

<table>
<thead>
<tr>
<th>CRP Concentration (mg/L)</th>
<th>Intra assay</th>
<th>Inter assay</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean value</td>
<td>CV (%)</td>
</tr>
<tr>
<td>5</td>
<td>4.9</td>
<td>4.2</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>2.3</td>
</tr>
<tr>
<td>250</td>
<td>251.3</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Correlation Studies

I-CHROMA CRP assay method compares with Abbot Architect Ci8200 Linear Regression
R = 0.905:

I-CHROMA CRP assay method compares with Toshiba TBA 200FR Linear Regression
R = 0.987 (see graph below):

For more information:
Call 00 44 (0)1869 238331  www.jbconsultingmdp.co.uk  Email John.bolodeoku@jbconsultingmdp.com

1. Boditech Med Inc. CRP assay datasheet
2. C. Anyaechi, A. Wyatt, J. Bolodeoku - Comparison of a Point of Care Test (POCT), iCHROMA™ C-Reactive Protein (CRP) assay method with the Abbott Architect Ci8200 CRP assay method, FOCUS 2016 (abstract number 123)
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The Editor is responsible for the final content. Views expressed are not necessarily those of the ACB.

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Front cover: Jonathan Berg has edited every edition of ACB News since July 1988 and this is it! Photo: Raj Garcha
The last year has been an eventful one for ACB News to report on. We have seen the move across England to drive forward networks based on the NHS STP regions. We have reported on this and other aspects of what is going on both in the Association and also the wider clinical science world around us.

For the final time at the end of 2016 I would like to thank everyone who has helped on ACB News over the last year. To the Associate Editors, their help for providing editorial and proof-reading. Also to our anonymous crossword and Sudoku compiler who never fails to deliver or indeed inspire.

Nikki Williams, Sue Ojakowa and Barbara Berg have worked unstintingly to help the Editor produce the magazine on time, every month; indeed after 341 consecutive monthly issues we have done that every single edition.

Editor Goes Walking

There is never a good time to give up doing something that has become a significant part of your life. ACB News has helped me develop marketing and publishing skills that are great fun to apply. For me there are new projects to take on that the many hours at home each month of ACB News work has not allowed. If you are ever in Birmingham and fancy a walking tour just book one here, www.positivelybirmingham.co.uk, where you might just spend some quality time with the ex-Editor of ACB News, where his sideways look at life continues!

End of a Busy Year . . . and an Era

Jonathan Berg
ACB News Editor, July 1988 – December 2016

ACB News 2017

In 2017 ACB News will move from monthly to bi-monthly publication. If you would like to send editorial in for consideration please use the email: editor.acbnews@acb.org.uk

If you are considering advertising in ACB News then please discuss your requirements with Sue Ojakowa at email: mail@prassoc.co.uk
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Annals of Clinical Biochemistry gets a Full Makeover

Edmund Lamb, Editor

Readers may be surprised when the Annals arrives in the post in January. Over the last few months we have been working with our publisher, SAGE, to develop a new design for the cover of Annals. The present cover has been in use, with minor modification, since 2002 and it was felt that it was time for a change. SAGE circulated a variety of possible designs which were refined by members of the Editorial Board. We hope that you like the chosen design, which we feel presents a refreshing and more contemporary image of the Journal.

Other changes are also afoot. After eight years as Editor-in-Chief I feel that both the Annals and myself should have a change. I am delighted that Dr Michael Murphy, who has been Deputy Editor for the last few years, has agreed to take over the EIC role with effect from January 2017. It has been an absolute privilege and honour to have been EIC of the Annals. I would like to thank all of the Editors and Editorial Board members I have worked with over the years, in addition to the ACB Office staff and the team at SAGE for the fantastic support I have received. I must also thank the Association’s Clinical Sciences Reviews Committee who have provided a continual stream of high quality topical reviews for publication in the Annals. I am confident that the Journal is being left in safe hands and will go from strength to strength.

Upon Reflection

If I may be allowed a short reflection, I hope we have also moved the Journal forwards in the last few years. In 2013 the entire back catalogue of the Annals back to 1960 was digitized, creating a fantastic resource for members. Starting in January 2016, access to the Journal after 1-2 years was opened up: it is hoped that this will improve visibility and impact of the journal over time and the early signs are certainly that there has been a dramatic (approximately three-fold) increase in electronic access (e.g. 250,000 full text downloads in 2016 by the end of September). Current volume and previous volume remain subscriber only. The impact factor of the journal has been maintained above 2.00 for the last three years, which is a first for the journal; article submission rates are increasing whilst the overall acceptance rate of the journal has been maintained at a healthy level of approximately 40%. Initiatives such as OnlineFirst and Annals Express have facilitated more timely publication of research articles and we have introduced TOC (Table of Contents) alerts for members as new issues are
released. Other improvements include the appointment of Associate Editors in the fields of haematology, immunology and, very recently, microbiology, broadening the appeal and scope of the Journal. We hope that the journal continues to meet your needs, but we are always open to suggestions for improvements and, of course, please keep sending your research papers to us for consideration.

Subscribers/members should also note that currently the Journal is being migrated from the HighWire platform to the Atypon Literatum platform, and the web address of the Journal will become: http://journals.sagepub.com/home/acb

**Annals of Clinical Biochemistry Seeks New Associate Editor**

The Annals now requires a new Associate Editor to join the team and help take the Journal forwards. This exciting role provides an opportunity for an experienced member of the profession to become involved with, and gain experience of, scientific publishing and contribute to the success and value of the journal.

All applicants will be considered although typically you will have an active publication record, and therefore a broad understanding of the publishing process, and be working at a fairly senior level in the profession.

To discuss this role, please contact the new Editor-in-Chief, Dr Michael Murphy, Tel: 01382 383541 or email: m.j.murphy@dundee.ac.uk

Interested applicants should send their CV with a covering letter to Michael before 31st January 2017.
Focus 2017 Registration

The Invitation to Participate has been circulated with the December ACB News and the PDF can also be downloaded from the Focus ACB website.

Abstracts for the meeting should be received by 09:00 on Monday 16th January 2017 with all first authors being expected to register as delegates for Focus 2017 in Leeds.

Abstracts must include:
- Specific aims of the study.
- Methods used, if pertinent.
- Summarise results obtained.
- The conclusions reached.
- Statements such as ‘data will be presented’ or ‘results will be discussed’ may lead to a rejection.

During the abstract submission process, authors can also indicate whether they would like to be considered for an oral communication or for the ACB Medal Award.

The Scientific Programme Committee and Editor of the Proceedings of the meeting will review all submitted abstracts and their decision is final. Corresponding authors will be notified either way by the end February 2017. Abstracts accepted for presentation will be published in a supplement to the Annals of Clinical Biochemistry.

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Sudoku

This month’s puzzle

Last month’s solution

MSRYITCHEH
HTYCREMIS
EICMHSRY
TMETHCRSYI
RCSIYHHTM
YHISTMECR
CRHEMIYST
SETRYCIMH
IYMTSHREC
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The Beer-Lambert equation relates concentration to absorbance:

\[ A = a \times b \times c \]

where

\[ A = \text{absorbance} = \log_{10} \frac{100}{36} = \log_{10} \frac{100}{36} = \log_{10} 2.778 = 0.444 \]

- \( a = \text{molar absorptivity} = \text{unknown} \)
- \( b = \text{light path} = 1.0 \text{ cm} \)
- \( c = \text{concentration} = 1 \text{ in 5 dilution of 250 mg/L} = 50 \text{ mg/L} = 0.050 \text{ g/L} \)

Convert to mol/L since molar absorptivity is required:

First calculate MW of NADH:

\[
\begin{align*}
C_{21} &= 12 \times 21 = 252 \\
H_{27} &= 1 \times 27 = 27 \\
N_7 &= 14 \times 7 = 98 \\
O_{14} &= 16 \times 14 = 224 \\
P_2 &= 31 \times 2 = 62 \\
Na_2 &= 23 \times 2 = 46 \\
\text{Total} &= 709 \\
\end{align*}
\]

Concentration (mol/L) = \( \frac{\text{Concentration (g/L)}}{\text{MW}} \) = \( \frac{0.050}{709} \) = 0.0000705 mol/L

a) Substitute these values and solve for \( a \):

\[
0.444 = a \times 1 \times 0.0000705
\]

\[
a = \frac{0.444}{0.0000705 \times 1} = 6298 \text{ L.mol}^{-1}\text{.cm}^{-1}
\]

or \( 6.3 \times 10^3 \text{ L.mol}^{-1}\text{.cm}^{-1} \) (to 2 sig figs since %T only given to 2 figs)
b) Use the Beer Lambert equation to calculate the final concentration which will give an absorbance of 0.5 in a cell with a path length of 0.5 cm:

\[
A = 0.5 \quad a = 6.3 \times 10^3 \text{ L.mol}^{-1} \text{.cm}^{-1} \quad b = 0.5 \text{ cm} \quad c = \text{unknown (mol/L)}
\]

\[
0.5 = 6.3 \times 10^3 \times 0.5 \times c
\]

\[
c = \frac{0.5}{6.3 \times 10^3 \times 0.5} = 0.000159 \text{ mol/L}
\]

Volume required = \( \frac{\text{Required concentration} \times \text{Required volume}}{\text{Stock concentration}} \)

Stock concentration = 5 x 0.0000705 = 0.0003525 mol/L (since it was diluted 1 in 5)

Therefore volume required = \( \frac{0.000159 \times 1000}{0.0003525} \)

\[= 450 \text{ mL} \quad \text{(to 2 sig figs)} \]

**Question 188**

The table shows data for two urinary screening tests for the detection of phaeochromocytoma:

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VMA</td>
<td>96.7</td>
<td>99.1</td>
</tr>
<tr>
<td>Total metanephrines</td>
<td>100</td>
<td>98</td>
</tr>
</tbody>
</table>

The prevalence of phaeochromocytoma in a hypertensive population is known to be 0.5%.

For a hypertensive individual calculate the probability of phaeochromocytoma being present:

a) Before either test is performed
b) If the VMA test is positive
c) If the total metanephrine test is positive
British Biochemists Win the Open!

Ian Watson, ACB Golf Co-ordinator

The First British-Dutch Clinical Chemistry Golf Open held at Mottram Hall

A small, but committed group formed the ACB Golf Society and we have held matches this year; so were we ready to meet our Dutch counterparts led by Hans Janssen? A match was arranged at Mottram Hall, near Wilmslow, a long parkland and hilly course, 7000 yards, used in Championship qualifiers. Four Dutch and six British players teed-off on the 30th September 2016; the weather was sunny, with a little wind and no rain. The course was in great condition, though there was some fearsome rough in which to lose balls if shots were wayward.

Bill Fraser and I inaugurated the Gemmel Morgan Trophy for the player in the Open challenge to achieve the highest individual Stableford score. Older generations of Biochemists are aware of the significant contributions Gemmel made to the profession as Professor at Glasgow, and he was also a keen golfer. The winner was Graham White with 35 points; we will be revisiting his handicap!

The Dutch had created a team prize to be presented to the winning Captain, a rather unique item as you can see from the picture!

The British team were clear winners. In mitigation:

- The Dutch had got up really early to fly to Manchester.
- In Britain the maximum male handicap is 28, in Europe higher handicaps are allowed. Application of this affected three of the Dutch players.
- Distances here are in yards as opposed to metres; and
- Maurits was playing with borrowed clubs.

Rajeev won both the Nearest the Pin and Longest Drive prizes.

Prizes were awarded at dinner (yet another excellent steak pie meal) and a convivial time was had by all.

It was agreed that this had been most enjoyable and that we had to have a return match, not least so that our Dutch friends could try and wrestle the prize from us. We have provisionally agreed 22nd September 2017 as the date, course yet to be confirmed, but possibly near Delft.

The ACBGS intend holding a Spring and Summer meeting hosted by Graham/Pete and Bill respectively i.e. South coast and Norfolk. If you want to join us contact me, Ian Watson, at iandwat@me.com

---

Ready to tee-off! Maurits Pekelharing, Rajeev Srinastava, Huib Storm, Pete Wood, Dinesh Talwar, Graham White, Fokke Posma, Hans Janssen, Ian Watson (Bill Fraser was held up on the M6, but made it with 2 minutes to spare!)

---

Hans Janssen hands the Open Trophy prize to Bill Fraser Captain of the victorious British team
ACB Wales Autumn Scientific Meeting

Joanna Flatt, Cardiff

The ACB Wales Autumn Scientific meeting was held on 13th October 2016 at the Holiday Inn in Newport. All of the attendees arrived on time, despite the potentially problematic existence of a second Holiday Inn elsewhere in the city!

ACB Wales Members’ Award

The meeting started with the Members’ Award presentations given by four Trainees. The first talk was a case presentation by Sally Thirkettle (Cwm Taf) entitled “The importance of Genetics in routine Biochemistry”. Sally presented an example of an 18 year-long misdiagnosis of type 2 diabetes, which was subsequently identified to be a case of maturity-onset diabetes of the young (MODY). Genetic testing confirmed the mutation in HNF1 in the proband and family members. This led to a new tailored treatment regime and improved glycaemic control.

A presentation on the complications from micronutrient deficiency following bariatric surgery was given by Helen Cordy (Cardiff and Vale). Helen presented the case of a woman who had undergone biliary pancreatic diversion surgery. She presented to hospital 6 years later with a low impact fracture and other symptoms, including loss of night vision. Laboratory testing revealed that she had low albumin and was deficient in numerous vitamins and trace elements. The poor outcome of this case highlighted the importance of planning treatment and follow-up prior to surgery in order to avoid the long-term metabolic complications of weight-loss surgery.

Jacqui Foulkes (Abertawe Bro Morgannwg), described her work to develop a unified Q-Pulse-based EQA process across all the departments in Laboratory Medicine in preparation for their move to ISO accreditation. Some of the challenges included differing local procedures, non-submission of results, not booking EQA samples onto LIMS, not reviewing or investigating non-conformances and not documenting the EQA process. The newly-developed Q-Pulse process currently being trialled has improved matters but some challenges remain.

The final speaker in the Members’ Award session was Liz Palmer (Abertawe Bro Morgannwg) who presented “A case of extreme hypercortisolaemia”. This 25 year old patient presented with low mood, anxiety,
acne and epigastric pain. Random serum cortisol was extremely high (>1750 nmol/L). There were concerns of interference but further, extensive (!), testing was consistent with ACTH-dependent Cushing’s Syndrome. The origin of the excessive ACTH remains to be determined.

All of the talks in this session were well presented and provoked interesting discussions and debate. The judges commented that they had found it very difficult to choose a winner, but it had to be done and the award was presented to Jacqui Foulkes by Mark Upton from Oxford Biosystems for her excellent talk, “Introduction of a pan-Laboratory Medicine EQA process”.

Liver Disease
Following the award presentations there was a return to the floor by Helen Cordy, who covered risk factors for liver disease, which is particularly relevant at the moment as mortality from liver disease is increasing year-on-year. This presentation was very useful in covering the various causes, stages, and complications of liver disease. Non-alcoholic fatty liver disease (NAFLD) is becoming more of a problem as we see increases in obesity and metabolic syndrome, but current blood tests are not particularly useful in these patients. Helen introduced the Liver Disease Plan from the Welsh Government and how this has been incorporated in Cardiff with an algorithm for investigating liver dysfunction. She concluded by presenting a clinical case in which a patient with alcoholic liver disease was also found to have underlying primary biliary cirrhosis.

Following the lunch break we were given food for thought in an engaging talk by Andrew Yeoman (Aneurin Bevan), who discussed the delivery of the Liver Disease Plan for the South West.
Plan for NHS Wales and improving early detection and prevention of liver disease. He highlighted that only 3-4% of people with abnormal LFTs have liver disease and that repeating these tests in a few months time is not useful clinically. Generally, the most difficult patients show only mildly abnormal LFTs over a long period of time, and in 60% of cases cirrhosis is only discovered upon admission for liver failure. Andrew is an advocate of using the AST:ALT ratio as it is has a good negative predictive value when less than 1, and is a more useful indicator of fibrosis risk than current LFTs.

Following on, Catherine Bailey from Aneurin Bevan described the practical aspects of implementing the Liver Disease Plan algorithm in their laboratory, which went live in July. In anticipation of this change, an audit of 2 years of data was carried out to identify the potential impact. It was found that there was an estimated 6,000 unnecessary LFT repeats on a group of 12,000 patients over just one month. The new algorithm reflexes AST measurement onto first-time raised ALT results in primary care patients, which represents approximately 6-8% of LFTs. There have been significant cost implications of increased specialist liver testing, along with increased AST testing. Referrals to Hepatology have not always been followed up and some received repeat LFTs, so there is more work to be done to get the message out to primary care.

**AFP Monitoring in Haemochromatosis**

The next talk was by Helen Jackson, also from Aneurin Bevan, and covered an important cause of liver disease and the most common genetic disorder in Northern Europe, haemochromatosis. Typically, the effects of haemochromatosis appear later in life. The initial detectable biochemical change is an increase in transferrin saturation; serum ferritin rises later. Transferrin saturation can be variable depending on time of day and fasting status, and ferritin is raised in the acute phase response. Treatment for haemochromatosis is primarily by venesection although this does not reduce the risk of hepatocellular carcinoma, so serum AFP levels should be monitored. Haemochromatosis patients with very high serum ferritin levels are at high risk of liver complications and should be referred to Hepatology.

**Colorectal Cancer**

After the very interesting and current liver disease session, there followed an equally engaging session centred on another hot topic – colorectal cancer detection.

The first speaker in this session was Helen Bruce from Surrey Pathology Services. Helen highlighted the importance of an early diagnosis as 10% of GP patients complain of digestive symptoms, but emergency presentations are often the route to diagnosis. Helen’s talk focussed on faecal immunochemical testing (FIT) in symptomatic patients as an alternative to guaiac faecal occult blood testing (gFOBT), which has been used historically. The problems associated with gFOBT include that it is not specific for human Hb, results can be affected by consumption of red meat and peroxidise-containing vegetables, interpretation is subjective and it requires 3 separate samples. As a result, gFOBT has been largely discontinued over the last 10 years. FIT has advantages, as it shows greater specificity, requires only one sample, can be automated and has the potential to be developed as a point-of-care test. One of its main strengths is a high negative predictive value.

**New Nice Guidance Coming Soon**

Follow-up colonoscopy resources are scarce and the use of FIT would therefore successfully screen out patients and avoid unnecessary colonoscopies. New NICE guidance for colorectal cancer testing in symptomatic patients is expected to be published in April 2017. (Editor’s note: since this article was submitted, the draft NICE guidance is now available for comment: https://www.nice.org.uk/guidance/indevelopment/GID-DG10005/consultation/html-content). The next speaker was Hilary Williams, an Oncologist from Velindre Cancer Centre in Cardiff, who gave us a clinician’s perspective of cancer and its prevention and therapies. More
aggressive treatments and improved surgical techniques have improved survival. Fewer cancers are now considered inoperable, and other therapies are available in these cases. There is concern that clinical pathways are not set up for rapid diagnosis of colorectal cancer, and in this area the UK compares unfavourably with other countries. Potential contributing factors include low population awareness, barriers to patients attending the GP and GPs not pursuing the “exclude cancer” route of investigation for non-specific symptoms.

The final talk of the day came from Hayley Heard, who described the Welsh experience of introducing a bowel cancer screening programme. The current scheme invites 60-74 year olds to send a sample for first line testing (gFOBT).

Colonoscopy Capacity Issues
A positive test result is followed up by a telephone assessment with a specialist screening practitioner, then colonoscopy or CT is performed if indicated. Initial findings suggest 10% of patients who were referred for colonoscopy had cancer. One of the challenges faced by this project was that only 55% of invitees responded, and it was found that men from deprived areas in particular were less likely to participate. Colonoscopy capacity and waiting times are also a problem and the aim of expanding the invited age range to 50-74 can only be considered once this has improved. Planned future improvements include introducing an integrated polypectomy service and replacing the first line gFOBT with FIT.

It was an excellent day with very stimulating talks and discussion. Thanks must go to Julia Walsh for organising it all!

Flexible Working Article Elicits Large Response
The article by Rachel Wheeler and Sarah Beck has clearly caught people’s imagination with 171 responses to the survey so far. Sample comments give a feel for the sort of issues that people have

“I believe that all staff members should be encouraged to work flexible as male colleagues have stated that they don’t feel they could ask to work flexibly”

“Have been told our Trust flexible working policy is not worth the paper it is written on by somebody in a senior management position and struggling to get my requests taken seriously”

“Flexible working can benefit the department’s finances as if you only drop a day a week, they will often not employ anyone else and therefore make a saving!”

“There should be more flexibility in working hours and part-time working, primarily to accommodate working families as I see the career as ‘family unfriendly’. People in part-time roles receive fewer opportunities for training, development or promotion/progression. They are left to perform routine work with their skills and experience undervalued because they work part-time. Part-time jobs are rarely advertised, unless there is someone already in mind. Jobs advertised as full-time are often unwilling to consider part-time workers, dissuading some people from applying”

Survey closes on 31st December: www.surveymonkey.co.uk/r/Y6ZXD5V
Chemistry of Life in Sheffield

Ian Hanning, Hull

In October a meeting in Sheffield marked the retirement of Professor Jim Bonham. A theme that cropped up time and time again was ‘working together’. Many excellent examples of collaboration were given, both across laboratory and clinical disciplines and between screening centres around the world.

Dr Mick Henderson (Leeds and the Willink, Manchester) looked at the establishment and evolution of the Society for the Study of Inborn Errors of Metabolism meetings. This went back to 1962, when meetings were held between Clinical Biochemistry and Paediatrics at Manchester Royal Infirmary to discuss phenylketonuria, with the first SSIEM meeting held in 1964. Topics in the 1970s included organic acids and calcium and bone metabolism. Even in the 80s requests for organic acids were only accepted if the patient was acidotic and the samples had been frozen – it sounds like interpretation of the GC traces in those days was a fine art! Over the last 50 years there has been an explosion of knowledge and we now have next generation sequencing, metabolite repair pathways, ‘moonlighting’ enzymes to name but a few.

Extending Newborn Screening

Professor Brian Fowler (Basel and Zurich), described Jim’s involvement with European Research Network for the evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism. The goal of ERNDIM is to reach a consensus between European Biochemical Genetics Centres on reliable and standardised procedures for diagnosis, treatment and monitoring of inherited metabolic diseases. The first meeting of ERNDIM was in 1992 and currently they provide 13 EQA schemes. Quality of service has always been high on Jim’s agenda and he has always been involved with ERNDIM, currently being Scientific Adviser to Diagnostic Proficiency Testing (UK), and also a Trustee.

Dr Mark Sharrard (Paediatrician at Sheffield Children’s Hospital) guided us through Jim’s driving role behind the introduction of expanded newborn screening in the UK, going back to the announcement by the UK Health Minister on 7th February 2007 that newborn screening for medium chain acyl CoA dehydrogenase deficiency would be introduced. This followed the outcome of the pilot scheme involving six screening laboratories in England between 2004 and 2006. Progression involved collaboration with BIMG, MetBioNet, UKNSLN and UKNSC to initially consider the criteria for candidate disorders and then which disorders should be included in the expanded screening. In May 2014, the UK National Screening Committee announced that screening in England would be further extended to include homocystinuria, Maple Syrup Urine Disease,
Glutaric Aciduria type 1 and Isovaleric Aciduria. This was achieved, following major involvement by Jim, in January 2015.

Professor Paul Dimitri (Sheffield Children’s Hospital), revealed that in retirement Jim would be collaborating to explore the possibility of screening for congenital adrenal hyperplasia. He highlighted the problems associated with this, in particular, the high false positive rate if just using 17-hydroxyprogesterone. Jim has some ideas!

Other retirement interests include collaborating to introduce screening in a number of non-UK countries, involving advice, training, educational material and, of course, diagnostic testing and clinical support. All in all a very active retirement!

I must admit, I came away from this meeting feeling enthused – the day covered example after example where changes were driven through by Jim’s dogged perseverance. This is certainly what life as a Clinical Scientist should be, making a difference to the service and the associated benefits to patients. It was a pity that there were not more Trainees present to be inspired.

This meeting was a tribute to Jim’s career and his many achievements. I was amazed by how many similarities there were with my career – born in Jarrow, inspired by Steven Rose’s book ‘The Chemistry of Life’, BSc in Biochemistry then MSc from Newcastle, started in the Newcastle Lab in clinical biochemistry, but thereafter our careers diverged.

I end with a quote from Jim: ‘working with others, particularly across boundaries both national and between disciplines is crucial and hugely enjoyable’. ■
From Chaos to Harmony Takes Time

Gethin Roberts, Wales

It seems hard to believe that ten years have passed since I wrote a letter to ACB News on “apples and pears” and standardisation of reference ranges. Following this, Jonathan Berg kindly invited me to a meeting in Birmingham in January 2007 to join the Pathology Harmony initiative. Catching the 5.20 train from Aberystwyth (something which was to become very familiar) I arrived to meet a small group of likeminded laboratory staff from the West Midlands and also Jeff Seneviratne who brought similar ideas from the North West. Why were reference ranges for common biochemistry tests such a shambles across the UK and what practical positive action could be taken to improve the situation?

Following the meeting Jonathan managed to secure funding from the Department of Health, and UK Pathology Harmony suddenly became a serious enterprise. Over the next few months a substantial body of data was gathered on the test names, units and ranges for the majority of common general biochemistry investigations. From the data, and using an entirely pragmatic and consensus based approach, a set of recommendations for test names, units and ranges was developed. By mid 2007 there was a sufficient body of work to take to the professions with the aim of promoting Pathology Harmony as a UK initiative. The funding had allowed the construction of a website and production of professionally designed information material. However, I do recall that in those heady times the main impetus came from a small group of dedicated and enthusiastic individuals who saw the value of moving these ideas forward. Quite simply people who were prepared to get on and actually do something.

UK Delegates Voted on Phase I Work

With the support of the professions, and a lot more work, a meeting open to all labs in the
UK was held in November 2007. Here the first set of Harmony proposals were presented, and voted upon by the gathered delegates. In almost all cases the proposals were carried by a substantial majority and these then formed the basis of Pathology Harmony Phase 1.

Spurred on by the initial success the initiative was further expanded in the next few years to include other aspects of biochemistry such as paediatric proposals and tumour marker guidelines and also to expand into other disciplines, haematology and immunology – with varying degrees of success. A Phase 2 meeting was held in November 2009 with other disciplines represented, and a further tranche of recommendations were adopted.

Crucially, support was also gained from the ACB, IBMS and College of Pathologists to request adoption of the agreed ranges across the UK, with a target date of April 2011.

Following the success of the Phase 2 meeting there were a few other notable events. Firstly, the Guidance for Non-specialists for Tumour Marker Requesting led by Cathie Sturgeon and presented as a useful bookmark style summary. Secondly, the harmonisation of units for haemoglobin and MCHC to g/L in 2013.

**Has it Made a Difference?**

So, where has this all led us? Unsurprisingly not all laboratory professionals were on-board with the Pathology Harmony concept. These doubters, for various reasons – some genuinely scientific, but more often related to entrenched attitudes and a denial of the vulnerability of their own local position – were reluctant to adopt the new standard approach. Oddly, from my personal experience in Wales there was no huge resistance to the Harmony proposals, though I have the scars from other bruising attempts at standardisation. In Wales we were luckily in the process of configuration of a single pathology system. This provided an impetus to pursue the standardisation agenda, but even here there was some inertia, lack of timely communication and management of change at some sites. So I’m not surprised that without this impetus the adoption of the changes would be even slower.

Presently I have no idea how many UK labs...
have adopted Harmony ranges. Following the Haematology work, there were no further central meetings held, and there are no plans at present for future initiatives. The website, www.pathologyharmony.co.uk, is still active and accessible with all proposals and responses to various enquiries, but since there are no new proposals it now acts mainly as a reference resource. From the point of view of Biochemistry the main reason for lack of further activity is, I believe, the diminishing return to be gained: few remaining tests are suitable for the Harmony “treatment”. Even within Phase 2 we were pushing the boundaries. For example, with some of the enzyme assays, if the EQA data between platforms showed significant bias, we could go no further.

**Challenges to Proposed Changes**

More recently, and again not surprisingly, there have been challenges to the proposed ranges. Many are of limited clinical significance, but two deserve mention. First, the issue of the paediatric reference range for sodium was raised both in Northern Ireland and in Gwent in Wales. In the context of a child with adrenal insufficiency a marginally low sodium may be the only abnormality in the general biochemistry profile. Interpretation which may prompt further investigation requires an accurate reference range. In an excellent paper by Dodd *et al* (**Ann Clin Biochem** 2015, 52(1) 39-43) paediatric electrolyte ranges were examined in detail with robust statistical analysis. The conclusion was that for sodium the paediatric Harmony range is too wide, certainly for older children and teenagers. In response to this evidence the all Wales pathology system now has a lower limit of 135 mmol/L for paediatric sodium.

The second issue is the range for serum albumin which attempts to accommodate the use of both BCG and BCP estimation methods. Personally, I feel that the root of the problem is the continued use of BCG methods which have been known to be prone to interference from other serum proteins since the original manual assays; this is exacerbated by unsuitable incubation times on many analytical platforms. The only sensible way forward is adoption of BCP across the board and review of the range. This would confer some advantages particularly in the context of more accurate cut offs in liver function investigation.

**Chaotic Starting Point Needs to be Appreciated**

So, I hear some of you say, this just shows that Pathology Harmony was doomed to fail, just an exercise in smoke and mirrors with no science or statistics behind it. Not at all! If anyone believed that the Harmony ranges were the result of informed and detailed data gathering of “normal” patient results followed by robust statistical analysis then they have entirely missed the point. We would probably only now be debating adoption of a handful of new ranges after ten years’ work.

During my talk at the Phase 1 meeting I put up a slide attempting to explain the thinking. We were starting from a position of chaos with no unified policy for the test names, units or ranges. We weren’t able to change the chaos to harmony overnight, but by selecting the tests with limited bias between methods and platforms we could bring forward some rational proposals for consensus ranges which would form a basis for future standardisation; a first step in a new approach which encouraged use of standard ranges unless there were compelling reasons not to. In my slide this was the second stage – consensus. The third stage, or as I called it the “Nirvana of Harmony” was always, in my view, the result of refinement of the consensus range in the light of new evidence, exactly as described for sodium in the example above. The whole point was that once labs were in consensus these changes could be made nationally in an ordered way.

Sadly, in order to attain this state of inner enlightenment the final step of review and confirmation needs to be established. This would involve a team to examine the Harmony proposals and review them; also a structure for change control would need to be put in place recording evidence and dates for changes.
This is where Harmony starts to overlap with other National and International initiatives.

So, there you have it. Ten years down the line from the original concept what sort of success can we claim? Certainly the first concerted attempt to address the chaotic situation of lab test reporting which had gradually deteriorated since the 1960s. For the first time we faced up to the prevailing denial that all our ranges were fine and somehow magically been created to suit our local populations. We took a radical look at the problem and came up with solution which was professionally promoted and not imposed but democratically agreed. We were not aiming for a diktat or values set in stone but for a standardised approach which was long overdue. Mergers and shared LIMS systems helped to promote the idea. In Wales virtually all the proposals have been configured onto the new all Wales system. It’s important not to forget the test names, units, report comments and method recommendations which were also part of the work of Pathology Harmony. The tumour marker guidelines were also groundbreaking as a novel way of making clear up to date advice available to all.

This is an incomplete project for the reasons I have explained. Whether we can take Pathology Harmony forward after some years of inactivity or whether other initiatives can take its place is a matter for the Profession to decide. But it would be a great shame, and of no service to clinician or patient if the concept behind this project fails to be appreciated with the result that we drift back into the fragmented practices of the past.
Kevin Lawton

16th April 1939 – 2nd October 2016

Kevin was born in the Potteries region of England but soon moved to Southport where he was brought up and educated before attending Edinburgh University in 1958 to study Biochemistry. Following university Kevin returned to Merseyside and was almost lost to the Antipodes during the exodus that took place in the 1960s but just in time a job came up in the Pathology Laboratories at Alder Hey Children’s Hospital which fortunately caught his attention. Kevin then worked alongside the legendary Joe Ireland in the Biochemistry laboratory for six years before moving to Fazakerley Hospital (now Aintree) as a Senior Biochemist in 1968. He continued to work there, gaining promotion to Principal Biochemist, until his retirement in 2003.

Kevin was always committed to providing a high quality biochemistry service and was instrumental in setting up the ‘new’ AFP screening service for the detection of neural tube defects on site in the department in the late 1970s. This service was to remain Kevin’s responsibility until maternal serum screening stopped as a local service. In the late 1980s Fazakerley Hospital, now Aintree, introduced an Infertility Unit which soon required oestradiol, progesterone and HCG testing to be done as and when necessary. Kevin embraced this challenge with enthusiasm and took responsibility for setting this up in the laboratory, working together with embryologists from the Unit. Many a happy outcome was achieved by patients attending this Unit which Kevin was pleased and proud to be part of.

I had the pleasure of working with Kevin when I first arrived at Fazakerley as a basic grade biochemist in 1986. As I was straight from university and with no real knowledge of clinical biochemistry, Kevin would regularly steer me in the right direction. Often he would impart information that seemed contrary and left me thinking, sometimes for days, about what was said. This as it turned out, was Kevin’s way to make people think about what they were doing and left him chuckling in the corner as it had the desired effect on the rest of us!

Kevin was a very private person but was always a pleasure to work with and with fond memories we used to have chats about Scotland, horse riding and for some strange reason about Stoke City football Club, as being from that region originally, he remained a lifelong supporter of the team.

M.L.
My previous article in ACB News looked at the possibility of screening for viruses in surplus serum (Issue 607, November 2013). There was also a suggestion I might be the oldest Honorary Member of the ACB; now, at 97, I probably am.

The clinical chemistry laboratory is on the first line of defense against any lethal pandemic caused by nature or by man. Biodefense, and indeed all real defense, aims to abort the maximum credible event. Ebola was far from such a maximum event.

The recent Ebola outbreaks infected over 30,000 individuals and killed over 12,000 before it could be stopped by barrier nursing and quarantine. Over a dozen vaccines were developed, and none played any part in aborting the disease. More infectious and lethal viruses can now be synthesised in the laboratory. To date biodefense has been a failure.

We have ruled out biological warfare in the past because both sides could be killed. However a new type of vaccine, termed synonymous codon substitution, now allows specific live vaccines to be rapidly made. Thus one can make a sword and a shield at the same time.

In the early 1950s Russian scientists and a captured German Luftwaffa engineer named Zippe designed a new version of the gas centrifuge for uranium enrichment. I spent almost 15 years on redesigning it for virus purification including consultation with Sir John Cockroft in the UK. The programme was a technical success and most influenza vaccines are now made with my K-II ultracentrifuge. The Joint NIH AEC Zonal Centrifuge Programme that did the work was disbanded, however, when no major human cancer viruses were found.

At this point in time the world has no credible general anti-viral defense. This being the case I would suggest that a small committee be formed within the ACB to assemble information, evaluate it, and plan. I would be happy to contribute anything I can.

If this zonal technology were to have been applied to Ebola, infected cadavers would have been radiation sterilized, and the viral loads isolated to yield a killed vaccine for ring vaccination. Thus one would buy time by ring vaccination with a radiation-killed vaccine to make and distribute a live one. All the technology required to do this exists or can be built, but is not widely known.

In the US, our health care system is about to be fragmented, and one cannot imagine what would happen to a terrorized and fleeing population that is sick and starving and has more guns than people.

I hope the ACB finds time to give this some thought.

Norman Anderson, PhD
Viral Defense Foundation
ACB News Crossword

Set by Rugosa

Across
1 Patient argument (4)
3 Consultant elicits past problem with time off (10)
10 Separate pure culture (7)
11 Inform after complete circuit about making a small error (7)
12 Graduate temper (7)
13 Neck of Cervantes losing stakes before nine! (6)
15 Pallid woman possessed by beginnings of anorexia nervosa (5)
16 Primary oral allergen disrupted cell functional unit (9)
18 Re-enter as wandering New Yorker, for example (9)
21 Seamstress disposes of unwanted material (5)
23 Woman’s principal problem is Spanish viral infection (6)
25 Gene variants featuring in suspiciously parallel essays (7)
27 Stitched up, sued about initial prostate operation (7)
28 Old stringed instrument in air rewritten for one Tortelli (7)
29 Bias in a small volume anteceding old city a hundred years (10)
30 Stand for close (4)

Down
1 Calculation test queried cash transfer missing closing rate (3-7)
2 Tolerate discussions raised about doctor (7)
4 WHO essential medicine treats hypotension? Not so! (9)
5 Pain that makes upset parent narcoleptic (5)
6 OTC drug hopeful no good (7)
7 Got out of involved litigation first (7)
8 Alternate strongman wear (4)
9 Particle Faraday named taken into account in some way (6)
14 Get out, leave! Overgeneralises about improvement in disease process (10)
17 Formulate good criteria defining a branch of medicine (9)
19 No lie about careless replicates, they each show a wide range (7)
20 Person relying solely on experiment, sadly impercipient but not inept (7)
21 Body fluid avails breakdown process (6)
22 Gladly accept another fifty for the research trust (7)
24 Body fluid can make odours with oxygen (5)
26 Italian town included in wine-tasting tour (4)

Last month’s solution

ACB News Crossword

Set by Rugosa
Consultant Clinical Biochemist

Band 8C: £56,665 to £69,860 per annum – 37.5 hours per week, Permanent

This post offers the opportunity to join a team of medical consultants and principal clinical scientists within the Clyde Biochemistry sector of NHS Greater Glasgow and Clyde (NHSGGC). The role involves providing a consultant level clinical service including an expert consultative advisory service and scientific direction to the Clyde Biochemistry Department. You will also have responsibility for undertaking teaching and training of students, laboratory staff, nursing staff and medical staff to postgraduate standards.

The post is based primarily at the Royal Alexandra Hospital, Paisley which is a busy district general hospital and one of the 3 hub hospitals of NHSGGC. All NHSGGC laboratories are on the same Laboratory Information System (Telepath). The laboratory has a tracked analytical system with Abbott equipment under an NHSGGC managed service contract. There are two additional hospitals within Clyde Biochemistry (Inverclyde Royal and the Vale of Leven Hospitals) which have smaller Biochemistry laboratories. The Clyde laboratories process in total over 7 million tests per annum. About 50-60% of these tests are derived from General Practice.

Registered with the HCPC, you will possess a Degree (or equivalent) in Biochemistry, Chemistry or a relevant subject and a Master’s level qualification in Clinical and/or General Biochemistry. You will also have FRCPath and substantial experience in Clinical Biochemistry.

For further information, please contact Dr Colleen Ross, Head of Service on 0141 314 6056 or colleen.ross@ggc.scot.nhs.uk

To apply visit www.jobs.scot.nhs.uk and search for job reference: 45168G.

The closing date for the post will be 13 January 2017.
Focus 2017 will take place at the Royal Armouries in Leeds. Set in a modern waterfront development close to Leeds city centre the Royal Armouries is home to the national collection of arms and armour, and displays over 8,500 objects throughout its six themed galleries.

The ACB Focus 2017 scientific programme, venue information, abstracts and daily updates will all be available in the palm of your hand on the free ACB Focus 2017 App for iPhone, Android and Windows. The exhibition will be situated on the main floor of the conference venue and will host the poster area and catering outlets.

The conference dinner will be held on the evening of 4th May.

The scientific programme includes plenary lectures, symposia and workshops along with oral and poster presentations. There are two symposia designed to celebrate contributions made by young scientists and medics.

We would encourage clinical scientists, medical consultants, medical trainees, biomedical scientists, medical students and postgraduates in laboratory medicine all to attend. There will be discounts for ACB members in training.

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