

# ACBNews

The Association for Clinical Biochemistry | Issue 585 | January 2012



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Value Chain

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Courses



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# ACB News

The monthly magazine for clinical science

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*Front cover: Some of our current trainees on the steps of the College.  
"Don't forget us with all this stuff about MSC" they said to ACB News!*

**Focus**  
Association for Clinical Biochemistry  
National Meeting  
Liverpool 2012

**focus on the patient**  
[www.focus-acb.org.uk](http://www.focus-acb.org.uk)

The Arena  
& Convention  
Centre, Liverpool  
30 April - 3 May

## ACB Foundation Award Lecture

**Tuesday 1st May 2012, Liverpool Focus**

The ACB Foundation Lecture Award at Focus 2012 entitled "Defining a diet for life – the role of the laboratory " will be delivered by Professor Ian Young from Belfast and it promises to be a lecture not to be missed. Ian Young is Professor of Medicine and Director of the Centre for Public Health at Queen's University Belfast. He works as a Consultant Chemical

Pathologist at Belfast Health and Social Care Trust, specialising in lipid metabolism and nutrition.

He has published over 300 scientific papers on topics related to nutrition and lipids, with a particular focus on oxidative stress. He is Associate Editor of Clinical Chemistry, Chair of the Scientific Division of the International Federation for



Clinical Chemistry and Laboratory Medicine, and a member of the Department of Health's Scientific Advisory Committee on Nutrition. ■

## LC-MS/MS Special Interest Group

The ACB Scientific Committee has requested that specialist interest groups should be organised to address issues in key areas of clinical biochemistry. The LC-MS/MS group was one of the initially proposed groups with a remit to provide guidance and advice on the safe implementation and operation of LC-MS/MS in clinical laboratories. The group will also address key issues such as standardisation of assays between laboratories. The LC-MS/MS group is being launched at an inaugural meeting to be held at the Royal College of Pathologists in London on Friday 12th April. This meeting will be an opportunity to meet members of the group

and listen to a number of invited speakers on relevant topics.

The Scientific Committee is seeking volunteers to become part of the LC-MS/MS group which is being chaired by Neil Leaver. It is envisaged that the group would aim to meet at least twice a year, with other communications via email and conference calls. If you have at least 3 years experience of LC-MS/MS and would like to be involved in the group please contact Alexandra Yates ([alexandra.yates@uhns.nhs.uk](mailto:alexandra.yates@uhns.nhs.uk)) or Neil Leaver ([n.leaver@rbht.nhs.uk](mailto:n.leaver@rbht.nhs.uk)) with a short statement outlining your suitability for participation in this group. ■

## Sudoku

### This month's puzzle

	Y					E	H
E					M		C
C					I		
	S	I	E		T		
			C		R	H	T
			S				M
M			I				Y
	I	T					C

### Last month's solution

T	S	C	E	M	I	H	Y	R
R	E	M	H	Y	C	I	T	S
I	Y	H	S	R	T	M	E	C
Y	M	I	R	T	E	C	S	H
C	H	E	M	I	S	T	R	Y
S	T	R	Y	C	H	E	I	M
E	R	S	I	H	M	Y	C	T
H	I	T	C	S	Y	R	M	E
M	C	Y	T	E	R	S	H	I

# ACB Spotlight Series



## Aspects of Hypertension and Infertility

Friday 10th February 2012

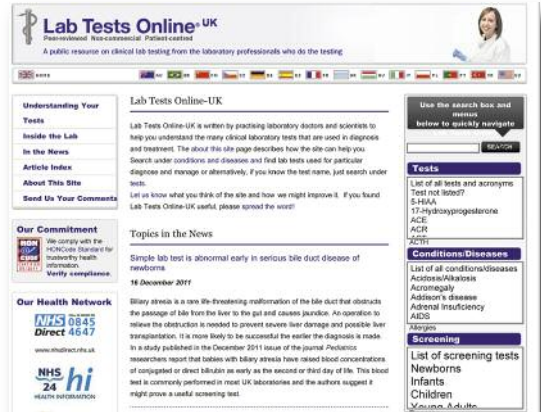
Royal College of Pathologists,  
London

Presentations include:

- ♦ Hypertension Overview  
*Professor Morris Brown, Cambridge*
- ♦ One in Half a Billion: An Unusual Case of Incidental Hypokalaemia  
*Dr Danielle Freedman, Luton*
- ♦ Mineralocorticoids  
*Professor Paul Stewart, Birmingham*
- ♦ Sub Fertility Overview
- ♦ PCO  
*Professor Steve Atkin, Hull*
- ♦ Case of Late Onset 21-OH Deficiency  
*Dr Stuart Smellie, Bishop Auckland*

For full programme and registration  
go to the ACB website meetings page:  
<http://www.acb.org.uk/site/meetings.asp>  
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[enquiries@acb.org.uk](mailto:enquiries@acb.org.uk)

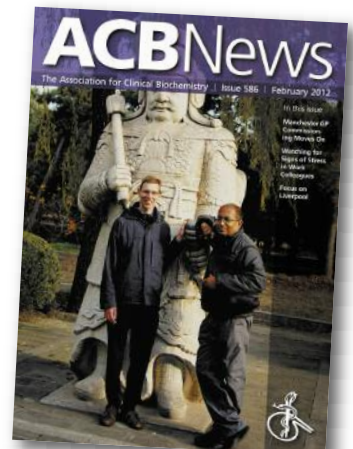
# New Chair Required for Lab Tests Online UK



Applications are invited for the position of Chair of the UK Management Board of Lab Tests Online (LTOL). LTOL is a website designed to provide the public with information written by professionals about clinical laboratory tests that are used to support clinical diagnosis and treatment. The UK version was launched in 2004 and is produced by the ACB in collaboration with AACC. If interested in leading and developing this successful initiative please contact Ruth Lapworth, Director of Publications & Communications before **Friday 10th February 2012**. ■

## Coming Next Month

We hope to look at the process being used to take forward tendering of GP work in Eastern England in February now. We will also be publishing comments of College examiners on recent examination papers. We will be considering some key issues in microbiology. If you would like to contribute articles to ACB News then do contact the Editor to discuss your ideas. ■



# Deacon's Challenge

## No 128 - Answer

A newly diagnosed epileptic commenced treatment with a daily oral phenytoin dose of 150 mg. After 2 months of treatment his average steady state plasma phenytoin concentration was 4.1 mg/L. Since there had been little clinical improvement the dose was increased to 200 mg per day and after a further 2 month period the new plasma phenytoin concentration was 7.5 mg/L. However, seizure control was still not ideal and the Neurologist has asked you to calculate the expected plasma phenytoin concentration if the dose is further increased to 250 mg.

Assume that phenytoin clearance follows saturation kinetics and bioavailability,  $F = 1$ , salt conversion factor,  $S = 0.92$  and the dosing interval,  $\tau = 24$  h.

Phenytoin is metabolised by hepatic oxidases which may become saturated. Therefore the rate of metabolism is non-linearly related to dose and mirrors the Michaelis-Menten equation used in enzyme kinetics:

$$v = \frac{V_{\max} [s]}{K_m + [s]}$$

In a steady state,  $[s]$  = average plasma concentration of the drug,  $C_{ss}$ , and the rate of metabolism must be equal to the rate of administration, which is given by  $F \times S \times \text{Dose}/\tau$ . Substituting these into the Michaelis-Menten equation gives the useful expression:

$$\frac{F \times S \times \text{Dose}}{\tau} = \frac{V_{\max} C_{ss}}{K_m + C_{ss}}$$

Calculation of the plasma steady state concentration when the dose is increased to 250 mg requires knowledge of the constants  $F$ ,  $S$ ,  $K_m$  and  $V_{\max}$ . Only the first two are given but values for  $K_m$  and  $V_{\max}$  can be calculated from the two simultaneous equations which results when two pairs of values for dose and  $C_{ss}$  are substituted into the above equation. For simplicity it is best to work with one of the linear transformations of the Michaelis-Menten equation (it doesn't matter which one). The double reciprocal transformation of Lineweaver & Burk gives the following equation:

$$\frac{\tau}{F \times S \times \text{Dose}} = \frac{K_m}{V_{\max} C_{ss}} + \frac{1}{V_{\max}}$$

When dose = 150 mg,  $C_{ss} = 4.1$  mg/L, therefore

$$\frac{24}{1 \times 0.92 \times 150} = \frac{K_m}{4.1 V_{\max}} + \frac{1}{V_{\max}}$$

and when dose = 200 mg,  $C_{SS} = 7.5$  mg/L

$$\frac{24}{1 \times 0.92 \times 200} = \frac{K_m}{7.5 V_{max}} + \frac{1}{V_{max}}$$

Simplifying these two equations:

$$0.174 = \frac{0.244 K_m}{V_{max}} + \frac{1}{V_{max}}$$

and

$$0.130 = \frac{0.133 K_m}{V_{max}} + \frac{1}{V_{max}}$$

Subtraction of the second equation from the first eliminates the  $1/V_{max}$  term:

$$0.044 = 0.111 K_m / V_{max}$$

$$\text{Therefore } K_m / V_{max} = \frac{0.044}{0.111} = 0.396$$

Substitute this value for  $K_m / V_{max}$  into one of the simultaneous equations (it doesn't matter which) and solve for  $V_{max}$ . Using the first equation:

$$0.174 = 0.244 \times 0.396 + \frac{1}{V_{max}}$$

$$\frac{1}{V_{max}} = 0.174 - (0.244 \times 0.396) = 0.174 - 0.0966 = 0.0774$$

$$V_{max} = 1/0.0774 = 12.9 \text{ mg/h/L}$$

Substitute this value into  $K_m / V_{max} = 0.396$  and solve for  $K_m$ :

$$\frac{K_m}{12.9} = 0.396$$

$$K_m = 0.396 \times 12.9 = 5.1 \text{ mg/L}$$

To calculate the plasma concentration at the new dose of 250 mg substitute dose = 250 mg,  $F = 1$ ,  $S = 0.92$ ,  $\tau = 24$  h,  $K_m = 5.1$  mg/L and  $V_{max} = 12.9$  mg/h/L into the Michaelis-Menten equation, and solve for the  $C_{SS}$  term:

$$\frac{1 \times 0.92 \times 250}{24} = \frac{12.9 \times C_{SS}}{5.1 + C_{SS}}$$

$$9.58 = \frac{12.9 \times C_{SS}}{5.1 + C_{SS}}$$

$$9.58 (5.1 + C_{SS}) = 12.9 \times C_{SS}$$

$$48.9 + 9.58 C_{SS} = 12.9 \times C_{SS}$$

$$12.9 C_{SS} - 9.58 C_{SS} = 48.9 \text{ mg/L}$$

$$3.32 C_{SS} = 48.9 \text{ mg/L}$$

$$C_{SS} = \frac{48.9}{3.32} = 15 \text{ mg/L (to 2 sig figs)}$$

Note that as metabolism becomes saturated a relatively small increase in phenytoin dose results in a marked increase in plasma concentration. ■

## Question 129

A 22 year old man (body weight 75 Kg) was referred to a Neurologist by his GP with a history of 8 seizures over the previous 3 months. He was previously successfully treated for grand mal epilepsy for many years with sodium phenytoin 100 mg bd. After obtaining a trough plasma phenytoin level of 8 mg/L the Neurologist increased the dose to 150 mg bd. However, the patient misunderstood the Neurologist's instructions and continued to take his old tablets in addition to his new dose (so that he was actually taking 250 mg bd). Over the next few weeks he became increasingly unwell, complaining of tiredness, nausea and vomiting. In A&E nystagmus was noted, a plasma phenytoin level (30 mg/L) confirmed phenytoin toxicity and medication was stopped immediately. The Neurologist has asked you to estimate how long it will take for the plasma level to return to the relatively safe concentration of 10 mg/L by endogenous clearance alone, at which point medication will be resumed.

Assume a volume of distribution of 0.65 L/Kg, normal renal and hepatic function and that phenytoin clearance follows saturation kinetics. Using the direct linear plot of Mullen to evaluate previous data, his  $K_m$  was estimated at 5.0 mg/L and  $V_{max}$  at 312 mg/24 h/total vol.

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# Controversies and Change in Immunoglobulin Assays

Dr Rachel Wheeler, St George's Hospital, London

## A report of the ACB Spotlight Meeting held on 2nd September 2011

On a beautiful sunny day, I reluctantly turned away from entering St James' Park in London, to head instead towards the Royal College of Pathologists for the ACB Spotlight Meeting on immunoglobulin assays. This was the first debates-style meeting that I had attended and it proved to be very rewarding.

### Should We Type Cryoglobulins?

In the first session, Dr Ravi Sargur (Sheffield) argued for the value of typing cryoglobulins. He reminded us that according to NEQAS, laboratory practice varies widely (*Clin Chem* 2008; 54: 39-43), but he believes that typing helps the clinician choose the appropriate treatment pathway in a reasonable timeframe and is ultimately cost-effective. Proposed surrogate markers, such as complement C4, are not reliable and wrongly assuming the cryoglobulin type could lead to significant delay in diagnosis e.g. of lymphoma, which can have legal consequences. Importantly, cryoprecipitates can be proteins other than immunoglobulins e.g. cryofibrinogen, fibronectin, CRP-albumin complexes, so simply reporting pos/neg could be mis-leading.

Dr M T Krishna (Birmingham) argued that typing of cryoglobulins is not routinely necessary, as clinical presentation and careful observation of the patient should be sufficient to achieve diagnosis and appropriate treatment. He pointed out that typing does not lead to definitive diagnosis because there is considerable overlap in clinical phenomena, although it can help in difficult cases.

Then came our first electronic vote. Once we had worked out how to use our handheld

devices, we voted firmly in favour of the motion that "cryoglobulins should always be typed" (56% for: 39% against). However, when the Chair, Dr Siraj Misbah amended the question to "cryoglobulins should be routinely typed", we were divided (50% for: 49% against).

### Serum Free Light Chains Aren't Cheap

After a quick coffee break, we took our seats for what many believed would be the most fiery session of the day: serum free light chains (SFLC), debated by Professor Mark Drayson (Birmingham) and Dr Joanna Sheldon (London). To the audience's disappointment, the two speakers mostly agreed on a lot of points, reviewed here:

- ◆ Quantification of paraproteins is highly variable between laboratories by any method.
- ◆ SFLC gives no information about the clonality of the free light chains.
- ◆ Electrophoresis and immunofixation is the only method that detects the clonality of free light chains. Both speakers value the routine analysis of serum and urine by this method in their laboratories.
- ◆ SFLC is a useful assay in some rare conditions, including non-secretory myeloma.
- ◆ SFLC is a very expensive assay.





But of course, the two speakers do have their differences. Professor Drayson favours wider use of SFLC in monitoring of patients, but still values analysis of urine at diagnosis. Dr Joanna Sheldon would like to see a more limited application of this expensive assay through close discussion with clinicians, rather than as part of routine investigation of immunoglobulins. On voting, the motion “serum free light chain measurement can replace urine measurements” was clearly

defeated (16% for: 81% against), a result that I think both speakers would agree with.

### Coeliac Disease

After lunch (and a quick stroll in the sunshine in St James’ Park), the third session of the day was an update on current tests available for investigation of coeliac disease.

From the laboratory perspective, Dr Bob Lock (Bristol) summarised all of the available tests and reminded us that there are clear NICE guidelines for which tests should and should not be used for coeliac disease. A new assay to detect antibodies to deamidated gliadin peptides is reasonably good according to a published meta-analysis (*Aliment Pharmacol Ther* 2010; 31:72), but still not as good as IgA anti-tissue transglutaminase (TTG) assay. Dr Lock also discussed IgA deficiency, a key issue in testing for coeliac disease as IgG autoantibodies must then be considered. He confirmed that IgA deficiency is defined as IgA <0.06 g/L and that even if the patient has very low but detectable IgA, IgA anti-TTG antibodies will be detected.

Dr Udi Shmuel (Northampton) shocked the audience by yelling “You bastard!” at us (though he was quoting a disgruntled patient from his Gastroenterology Clinic). He gave us an entertaining perspective from the clinic on the practical use of coeliac assays based on their positive and negative predictive values. In his experience, serology is used mainly to exclude coeliac disease, because the assays have a good negative predictive value.

### IgG4-Related Systemic disease

The final session of the day debated IgG4 in autoimmune disease. Dr Ross Sadler (Oxford) and Dr Emma Culver (Oxford) collaborate on this topic, so they struggled to disagree! Raised IgG4 concentrations were originally described in association with “autoimmune pancreatitis” but this has now been expanded to apply to a spectrum of diseases and syndromes, known as “IgG4-related systemic disease” (*Curr Op Rheumatol* 2011; 23:88). Two key features are (i) the presence on histology of infiltrates of plasma cells in the affected tissue which are positive for IgG4 but not



other immunoglobulins, and (ii) patients respond well to steroids. Dr Sadler presented data to suggest that measurement of IgG4 concentration is particularly useful for distinguishing pancreatic cancer (normal IgG4) from other pancreatic disease. Dr Culver revealed that many patients who meet the diagnostic criteria for these diseases have normal IgG4 concentrations, making measurement of IgG4 of limited diagnostic use. However, she agreed that it was useful for ruling out pancreatic cancer, which requires aggressive surgical treatment, though she also mentioned that autoimmune pancreatitis and pancreatic cancer can co-exist. This session was useful in updating us on this field, but so much remains to be discovered, particularly regarding the underlying pathology.

I really enjoyed the debate format of this meeting, as it is rare to hear conflicting views on the same subject presented at one event. Attendance by a mixture of clinicians and scientists from Immunology and Biochemistry enhanced the debates. Electronic voting adds an interesting element, though technology defeated us in the final vote, where the motion "IgG4 is useful in helping to diagnose

autoimmune disease" was passed by 'lots' to 'not very many'. I look forward to similar events in the future. ■



# Near Patient Testing in Microbiology

## ACB Spotlight Meeting - 10th October 2011

Derren Ready, *Associate Editor*

Dr Beryl Oppenheim chaired the day's sessions and allowed the audience to consider the implications of near patient testing for microbiology. She highlighted the importance of understanding training needs especially in areas with a high staff turnover, the service cost, workers resistance to change, the quality of the result and governance.

### Urinary Dipsticks

Dr Andrew Swann described the use of urinary dipsticks for the detection of urinary tract infections (UTIs) and suggested that there was evidence from UK general practice that urinary dipstick tests (nitrites, leukocytes and blood) can modestly improve the precision of UTI diagnosis. However, he reported that negative predictive values may be worse than expected as demonstrated in a study which reported that 24% of urine samples from women with dipstick-negative results were indeed culture-positive. Dr Swann suggested that the use of dipsticks was dependent on the patient group tested, with no robust evidence to support dipstick use when investigating UTIs in men, the over 65s and infants less than 3 months. However, he suggested that there was a potential role for their use in women with mild UTIs (antibiotics are recommended for the treatment of UTIs in women with severe symptoms or signs, regardless of the dipstick results), children aged 3 months to 3 years (if rapid microscopy was not available), children over the age of 3 years (nitrite-positive test results indicate UTIs) and patients with pyelonephritis (nitrite-positive and leukocyte esterase-positive results indicate UTIs).

### Rapid HIV Testing

An enlightening perspective was given by Dave Smith and Jane Brown when they described the realities of implementing HIV

testing into the community. They described the high anxiety for patients whilst waiting for their HIV result and therefore a same day result in a local setting was very appealing to a diverse population including gay, straight and multi-ethnic populations.

### Validation, Monitoring, Quality and Training

Gill Hall gave an excellent presentation that demonstrated the difficulties of providing an 'out of lab' service which was of CPA standard. The personnel, premises, equipment, appropriate storage of kits and the appropriate recording of patient details all provided different challenges which were often difficult to overcome. Gill recommended that training of the staff carrying out the POCT and robust validation of the results was essential to achieve a high standard service.

### RSV Testing: Benefits for Infection Control and Bed Management

Dr Kate Templeton a Consultant Clinical Scientist at Edinburgh Royal Infirmary, highlighted the role of POCT for respiratory pathogen detection. Again it was obvious that good quality training was essential to ensure that rapid, accurate POCT results could be obtained. Kate reminded us that the very young, aged one year and under, and the elderly are most at risk of developing severe illness due to respiratory syncytial virus (RSV). Premature neonates or children with underlying cardiac or chronic lung disease are at particular risk. She stated that if the clinician expected to admit the child then a naso-pharyngeal aspirate-RSV POCT would be carried out. Kate described that the use of the RSV POCT had good performance (90% sensitivity & 91% specificity), this allowed rapid detection of RSV, which in turn informed

local infection control procedures. If a patient was shown to harbour RSV they would be admitted to cohort. However, if the POCT test was negative then the cubical could be used for additional patient treatment. This policy saved the hospital a considerable number of inpatients requiring cubicles. Kate noted that in a cohort of 549 patients seen in A&E in 2010/11 95% had a viral diagnosis but only 65% of this was RSV so in the future a combined respiratory viral POCT assay could provide the best option for diagnosis and patient management.

Finally, Kate underlined the importance of external quality assurance, with monthly reporting and a focus on retraining staff if EQA was not of an acceptable standard.

### **MRSA POCT**

Dr Rohinton Mulla commented upon the clinical implications of those with MRSA infections. She stated that MRSA screening was carried out for patients as soon as possible after entry into the hospital and that these results should be available before the patient moves to their destination ward. Again the results of these investigations were able to inform local infection control procedures assisting in the decision to treat or isolate MRSA-positive patients. Dr Mulla highlighted the importance of good IT, training and the provision of robust, easy to follow protocols and stated that 66% of the results were available on the local computer system within 4 hours of admission. She had also carried out cost benefit analysis and these data suggested savings of approximately £350,000 per annum, by reducing reliance on culture and improving bed management.

### **Procalcitonin: Dream Biomarker or Just Another Nightmare?**

Dr Kate Adams, an infectious diseases clinician from Hull, described the potential use of pro-calcitonin testing (PCT) in patients with respiratory infections and those in critical care. She stated that serum levels of this biomarker

are generally elevated in bacterial infections, and tend to rise after 4-6 hour (earlier than CRP) and peak at 8-24 hours, the half-life is about 24 hours and levels will reduce by approximately 50% each day if the infection is resolving. Interestingly, the PCT levels do not appear to be affected by steroids or non-steroidal anti-inflammatories. However, Dr Adams did emphasize that PCT levels could be raised after surgery or trauma, in patients with pancreatitis, may not increase in localised or intracellular bacterial infections and cost £10 per test compared to £2 for a CRP test. Dr Adams did suggest that PCT levels could be used to inform antibiotic prescription, with levels of 0.5 ng/mL or above indicating the use of antibiotic therapy, and levels of 0.1 ng/mL or below preventing antibiotic use. She described previous data which had used PCT algorithms to inform antibiotic usage and showed that there had been a significant reduction in antibiotic use in the PCT groups.

### **Nearer Patient Testing: The Role of The On-site Laboratory**

Dr Sue Murray, a Consultant Clinical Scientist at the Royal United Hospital (RUH) in Bath, described the role of a small, on-site laboratory. The microbiology service at the RUH processes blood cultures, cerebrospinal fluids and other urgent specimens (fluids, tissues, corneal scrapes etc.); processing approximately 12,000 specimens are processed per year, with the other samples being sent to Bristol. Dr Murray described the key issues for a 'hot-lab' which included; the size and specialties of the hospital(s) served, management and training of the staff who may have a different employer from the host Trust, lone working, and on-call rotas. She emphasised the need for excellent IT and transportation links between the 'hot-labs' and main laboratory taking into account the distance to the main laboratory, the journey time and the frequency of sample collections (to complement GP sample arrivals) which were essential to get right. ■

# New Format for ACB National Training Courses

**Karen Mitchell, Education Committee**

In November 2012 a new format for the ACB Training Courses will be launched. The redesign has been stimulated by both the changes to training brought about by Modernising Scientific Careers (MSC) and feedback from both scientific and medical trainees. The aim is to offer a shorter, more focused course for trainees preparing to sit the FRCPATH examinations at a cost which is more attainable.

The new training courses will aim to cover topics not already covered by Masters Degree courses and will have a more interactive and practical aspect to them. They will cover the latest developments which have not yet made it into textbooks as well as subjects that are not easily covered by 'book learning'.

The courses will be held in November and June at the Warwick Conference Centre over 3 days (from lunchtime day 1 to lunchtime day 3) enabling trainees to travel at off-peak times and giving sufficient time to assimilate the new learning before the next round of exams.

## Rolling Programme of Four Courses

A sub-committee comprising Dr Frances Boa and Hazel Borthwick (Director and Deputy Director of Education, Training and Workforce), Dr Mark Sleeman (Chair, Trainees' Committee), John Shepherd (Yorkshire Regional Tutor) and Dr Karen Mitchell (Ordinary Member of the Education Committee and Medical Representative) have devised the new programme with reference to the FRCPATH Clinical Biochemistry and the MSC curriculums and the Microbiology and Immunology professional committees. The sub-committee will oversee the planning of the first course, and act as advisors for subsequent courses. The rolling programme of courses will run over 2 years (4 courses), each of which will be organised by a rotational regional committee, and held in a central location.

Each course will consist of generic components relevant to all members of the ACB, followed by parallel discipline specific sessions for Microbiology and Immunology trainees as required:

	Monday	Tuesday	Wednesday
Morning session		Generic teaching	Discipline specific teaching
Afternoon session	Start at ~ 13:00 Generic teaching	Discipline specific teaching	Finish at 13:00
Evening session	Generic workshop	Cases / Methods	
	Trainees' Evening	Dinner	

Course registration will be flexible to allow attendance for a single day (2 sessions), or the full course, and will be available with or

without accommodation as required.

The detailed programme for the first of the new courses in November is as follows:

	Monday	Tuesday	Wednesday
0900-0945		Research within the NHS	Interpretation and application of DFTs <i>*Microbiology TBA</i>
0945-1030		Break	Break
1100-1145		Communication skills for science	National Screening Programmes and their calculations <i>*Microbiology TBA</i>
1145-1230			
		Lunch	Lunch
1330-1415	IT within laboratories	Critical illness <i>*Microbiology TBA</i>	
1415-1500	Use of decision support systems		
	Break	Break	
1530-1615	Health and Safety	CSF Biochemistry – analysis and interpretation <i>*Microbiology TBA</i>	
1615-1700	Risk and COSHH assessments		
1700-1830	Dinner	Case / Methods	
1830-1930	Trainees' Evening	Dinner	

If you would like to register your interest as a participant on the new course, or if you would like to be involved with organising one of the new courses, please contact: ACB Administrative Office, 130-132 Tooley Street, London SE1 2TU. Tel 020 7403 8001 or email [enquires@acb.org.uk](mailto:enquires@acb.org.uk) ■

# An Inspiring and Inspirational Experience

Rebecca Leyland, Senior Clinical Biochemist, Royal Free Hampstead NHS Trust

## Rebecca reports on a second visit to the Vellore Christian Medical Centre in India

In 2010 Patrick Walker visited the Clinical Biochemistry Department at the Christian Medical College (CMC) in Vellore, Tamil Nadu, India. After hearing about Patrick's experience at CMC I was inspired to follow in his footsteps. Please refer to Patrick's article in issue 574 of the ACB News (Feb 2011) to gain an insight into his visit and the history of CMC. At the beginning of August I set off for my four week placement and despite Patrick's insight I was still unsure of what to expect having never visited India before. Nothing could have prepared me for the chaotic environment I found myself in as the hustle and bustle of Vellore engulfed all of my senses. At the hospital 6,183 outpatients are seen daily in addition to the 2,166 inpatients who are cared for and with 7,967 staff, it's as chaotic inside the gates of the hospital as it is on the road outside. Despite the busy exterior the hospital is run to exceptionally high standards and follows the 'both and' philosophy: "providing high-tech health modalities as well as cost-effective healthcare solutions".

### High-Tech Equipment for a High Workload

As Patrick described in his report the Clinical Biochemistry laboratory at CMC is well equipped with automated analysers for all the main chemistry and immunoassay tests, HbA1c analysers, an atomic absorption spectrophotometer and a recently installed ICP-MS to name but a few. Another recent addition to the laboratory is the VersaCell, a self-contained robotic arm connecting the



*The rural mobile clinic run from CHAD*

Siemens Immulite and Advia Centaur standalone analysers. All the samples from the main chemistry autoanalysers are put into the VersaCell, which reads the sample barcode and delivers the samples to either the Immulite or Centaur for testing. This eliminates the laborious process of sorting samples that require further testing and directing them to the correct immunoassay platform.

### First Rate Service in a Developing Country

In contrast to the hospital where I trained, which had a fully automated track system provided by a single manufacturer for routine work, the lab at CMC had chemistry analysers from two manufacturers and immunoassay platforms from three manufacturers. However, I soon discovered that unreliable reagent supply and technical support discourage labs

from 'putting all their eggs in one basket'. Also the reason why a number of reagents are prepared in house, a fundamental requirement when reagent supply is not guaranteed. In the UK there would be turmoil if a manufacturer couldn't supply a routine chemistry reagent for a couple of months, at CMC it's taken in their stride and strategies are in place to cope; they have to be.

Akin to most of the country the electricity supply in Vellore is sporadic and despite the hospital having its own generators to minimise the effects of this there are still a few power cuts every day. Fortunately the lab has a UPS system to maintain a constant uninterrupted electricity supply to all the analysers, but the lights and air-conditioning go off. Approximately one hundred large batteries occupy a room just outside the lab, not quite as compact as some UPS systems in the UK but they are sufficiently robust to handle the frequent usage. In addition to the intermittent power supply, the water supply in Vellore is limited with some areas of the town only receiving water as little as once a week. Despite it being the rainy season while I was there the local river bed and lake remained dry. Fortunately CMC source water from elsewhere and transport it in tankers to the hospital campus, where it is carefully used and recycled where possible. The lack of these essentials is a stark contrast to the UK where water and electricity supplies are seemingly unlimited.

### Experiencing Indian Clinical Biochemistry

During my placement I had the opportunity to gain experience of a number of techniques that I had not previously seen. The measurement of lead in whole blood by atomic absorption spectrophotometry was interesting owing to the general trend towards retirement of this method in the UK. The lab at CMC had recently purchased an ICP-MS and were working up methods for arsenic species, cobalt and copper while I was there.

CMC is one of only a few hospitals in India to offer sweat testing to aid the diagnosis of Cystic Fibrosis. Children and their families

travel from all over the country to be tested, with at least one sweat test performed every day. At CMC sweat collection is performed by a medical scientist from the lab, either in the department itself or at the patient's bedside. Using a member of staff from the lab ensures the strict procedures for sweat collection are followed and that the person performing the collection has sufficient experience as they undertake numerous tests every week.

The Clinical Biochemistry Department at CMC not only performs routine and specialised biochemistry tests but also a number of immunology and genetic tests. The department has a Roche Lightcycler which uses quantitative real-time PCR and melting-curve technology for mutation analysis. The department has methods for BRCA1, BRCA2 and P53 set up for use in breast cancer patients.

A national EQA scheme for chemistry analytes with 3000 participants is run by the Clinical Biochemistry Department at CMC. The distribution being prepared while I was there was the first using human serum instead of bovine serum. The blood bank provides the scheme with 17 L of plasma that would otherwise be disposed of. The first step is to transport the plasma to the department of nephrology where it is dialysed to remove excess electrolytes, glucose, urea and creatinine. As you can imagine, having a large container of plasma attached to a dialysis



*Clinical Biochemistry staff attending one of my seminars*

machine attracted quite a lot of attention from the clinical staff and patients on the ward. From the dialysis unit the plasma is taken back to the lab where a combination of calcium, sand and salt is added to promote clot formation and ultimately the transformation into serum. Analytes are spiked in to the serum to achieve the desired concentrations for the distribution and the serum is then ready for lyophilisation. The lyophilisation machine was reminiscent of something from Doctor Who. Over a period of forty-eight hours water is removed from the serum leaving powder in the base of the vials, ready for reconstitution by the participants. Another machine is then used to seal and label the samples ready for distribution to the 3000 participants across the country. If the power supply to the lyophilisation machine is lost at any point during the forty-eight hour process the damage to the samples is irreparable and the excruciating process must be started again from scratch, hence a member of staff attends to the machine for the whole process.



*The lyophilisation machine*

## Community Work at CMC

In addition to the main hospital CMC also has a number of community projects. I was lucky enough to experience some of the ways in which CMC fulfils its commitment to the provision of affordable healthcare to the local community. I accompanied one of the doctors from the low cost effective care unit (LCECU) into the slums of Vellore, I attended a rural clinic run by the clinicians at the Community Health and Development project (CHAD) and I also attended a diabetes clinic at the hospital. The projects all worked in different ways for a wide variety of patients. I met a young woman with schizophrenia, who owing to an injection of anti-psychotic medication given every two weeks by a community doctor, was able to integrate into the local community and have a good quality of life. Biochemistry in the community is quite different to that in the UK, the small lab at LCECU uses glucometers to measure fasting and postprandial glucose concentrations in diabetics, an alternative to the comparatively expensive HbA1c. Diabetes education sessions in the community are run by the Endocrinologists from CMC and involve a diabetic nurse, a clinician and the local cobbler. The latter not being someone we may consider with the colder climate and culture in the UK, where footwear is worn by the vast majority of the population, but in India the value of good footwear for diabetics is a vital part of diabetes education.

I thoroughly enjoyed my time at CMC and learnt a phenomenal amount about clinical biochemistry and healthcare in India. The experience also provided an invaluable opportunity to reflect on how clinical biochemistry operates in the UK and the considerable differences and similarities between the two countries. I would highly recommend the experience to other trainees and would like to take this opportunity to thank Professor Fleming, Professor Selva Kumar and all the staff in the clinical biochemistry lab at CMC for their kind welcome and the time and effort they put into making my experience so memorable. ■

# Addressing the Value Chain

Fiona Stratford and Nicola Seaward, Royal Gwent Hospital, Newport

## Here Nicola and Fiona give their personal highlights from the Roche-sponsored Value of Pathology Event

The Value of Pathology meeting was held at the Royal College of Pathologists and hosted by Roche. It focused on the role that pathology plays in the patient care pathway, how services will be delivered in the future and the impact this will have on the longer term quality of care delivered by pathology professionals.

### Setting the Scene

The meeting was introduced by Professor Peter Furness, President of the Royal College of Pathologists. He emphasised not only the common misconceptions surrounding pathology but also the increasing demand that the public and clinicians are likely to place on clinical pathology services in response to continuously evolving medical research. Using oncology as an example, he highlighted how increasing information on cancer genomes and the reduction in costs of DNA sequencing may mean that in the future, pathology will need to offer molecular biology assays as part of its repertoire. But are we ready for such increasing demand? This was the question posed and he emphasised that there is always room for improvement, highlighting Lord Carter's recommendation for an end-to-end pathology service which should be quality managed at all stages.

### Patient Facing for Pathology Excellence

Dr Jonathan Berg provided an interesting talk on the innovative approaches that can be undertaken to engage the public in pathology and improve public perceptions.



It was emphasised that the key to a successful patient facing service is improved communication. The huge interest in healthcare in the media can be used to our advantage, making the best use of websites, media releases for relevant journal articles and posters to increase the public's understanding of the value of clinical pathology, especially in light of the upcoming National Pathology Year 2012. Jonathan also demonstrated other key drivers including team building and cross-disciplinary interaction, maintaining basic pathology excellence, keeping up to date with technology, introducing creativity and innovation and ensuring good financial backing within the trust. In particular he pointed to the importance of establishing good relationships with financial directors. Considering the current economic climate, he also highlighted his concerns regarding laboratories that chose to behave in an unprofessional manner. For example, abruptly withdrawing work from their referral service providers without warning or explanation. In the light of this he emphasised the responsibilities attached to commercialisation in the public sector.

Examples of patient facing schemes included an alcohol awareness programme. This open access scheme on the streets of Birmingham

providing various tests associated with alcohol-related illness. Improving phlebotomy services in emergency medicine and implementation of a vitamin D blood spot test service to the public at SWBH NHS Trust were also discussed. The latter neatly overcomes the problem of demand management of the “worried well” wanting to know their vitamin D with a website allowing the public to purchase the test directly from the laboratory.

Jonathan finished by highlighting the importance of increasing awareness of the value of pathology amongst clinical staff and demonstrated how a programme using urea and creatinine can allow better assessment of hydration status on wards where dehydration can be a problem.

### **Value of Pathology - A GPs Perspective**

Dr Hemal Desai gave an illuminating presentation on what GPs really want from their pathology service. Dr Desai is an advisor

to the Department of Health for the commissioning of pathology services. He began his presentation with a discussion of what he views as the challenges facing pathology services. These included increasing demands for tests, the differing needs of primary and secondary care, the variable costs of services to the commissioners, the increasing demand for management of long-term conditions, implementation of QIPPs and, of course, the huge financial constraints that all departments face.

He then discussed the need for laboratories to market their services to GPs, who as customers have a choice where they purchase these services from and who in an increasingly difficult economic climate will demand value for money. Drawing on a model from industry “The value chain” he described how pathology services could add value to their service at all points in the pathology process from request to report.

Specifically he felt pathology could improve

*Some of the more junior delegates enjoyed having their photo taken on the College steps*



their services for primary care by streamlining the request process, improving access for patients to phlebotomy services, improving the transport system so that it fitted in better with GP schedules, developing a more coherent IT system so that GPs had access to pathology reports from secondary care, standardising the costs of tests and developing a service specifically for the needs of primary care rather than one focused around the needs of secondary care.

### Lab in Hemal's Pocket

As a GP, Hemal would like more point of care testing facilities. He described his vision for a "pocket lab" where assays could be performed quickly, cheaply and easily at GP surgeries and he felt this was a further area where laboratories could add value by advising and assisting primary care to set up these facilities.

In conclusion, he stated that commissioners of the future will want more value for money, not just in financial terms but also in terms of service. Therefore, laboratories will need to demonstrate the value of their services more tangibly.

### Gaining Control by Taking Ownership

Dr Martin Myers in his presentation "Delivering a Total Pathology Solution for the Future" picked up several of the themes outlined in the previous talk. Again he discussed the many and varied challenges facing pathology. These include the time-bomb of management of long-term conditions, the ever increasing demand for pathology tests, the lack of funding for new diagnostic tests, especially molecular biology tests. We also face the challenge of reducing expenditure in pathology when we already spend less in the UK on *in vitro* diagnostics per head of population than anywhere else in Europe and where we have already decreased the cost per test by an average of 20% over

the past 9 years. He described how over the same time period productivity has increased by a remarkable 76% and comparisons with countries such as the USA show that we provide a service of equal, if not better, quality in that we are less likely to produce incorrect results. Despite these reasons to celebrate UK pathology services Dr Myers suggested that by taking ownership of the whole pathway, improvements in pathology services could be made. In addition to focusing our attention on the analytical part of the process we need to gain control of phlebotomy, transport and IT. He discussed improvements that could be achieved in the future by changing the way we organise pathology services and the role of POCT, pathology harmonisation and smart commissioning in this process. He emphasised the importance of viewing the patient pathway as a whole. Using examples such as measurement of BNP in the diagnosis of heart failure he illustrated that by spending pennies on laboratory testing the NHS could save pounds by reducing the number of expensive procedures and outpatient visits.

### Bollywood Haematology Film Premiere

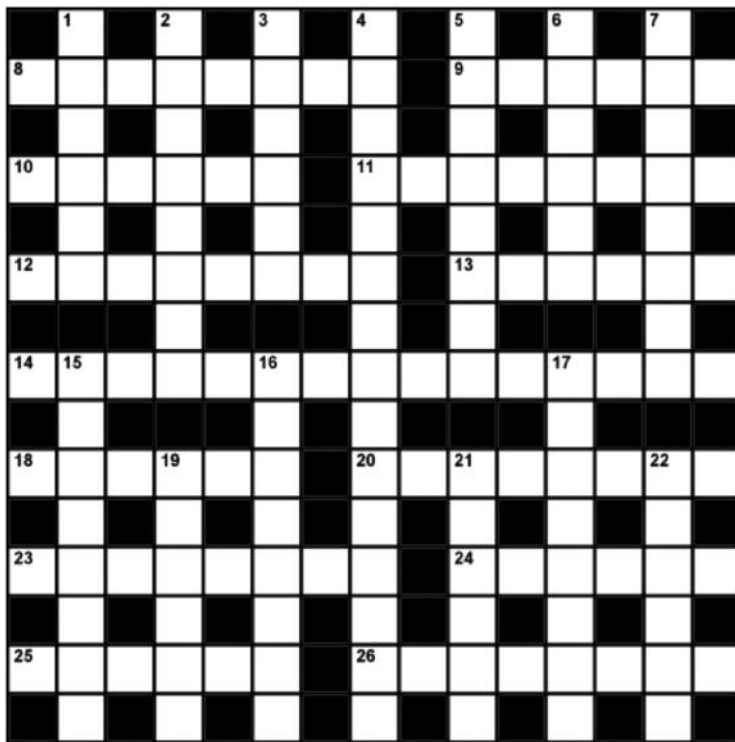
The meeting concluded with the premiere showing of the educational film "The Ultimate Goal" directed by and starring Dr Sivakumaran. This docu-drama demonstrates the crucial role pathology plays in providing clinicians with the information they need to diagnose and treat patients. It follows a work experience student as he rotates through all the pathology disciplines. It specifically shows the role of the Biomedical Scientists in the modern laboratory. The film will be distributed throughout schools and hospitals within the UK to educate others about the value of diagnostic tools and to promote clinical science as a career choice. ■

# ACB News Crossword

## Set by Rugosa

Keep sane at coffee time with the ACB News Crossword. Always relating to the science and practice of Clinical Chemistry, you will never cease to be astounded by the convoluted mind of the ACB News Crossword compiler.

Prizes for your department: The first five correct solutions to appear on the ACB News fax machine (Fax: 0121-507-5290) will receive a copy of the new educational Calcium Cases CD-ROM by Aubrey Blumsohn, Christina Gray, Neil McConnell, John O'Connor, Anne Pollock & Roy Sherwood and which retails at over £50. Please state clearly the name and address of the Department that is entering the competition. Remember that ACB News appears first as a PDF on [www.acb.org.uk](http://www.acb.org.uk) around the 7th of each month.



- 4 Resuscitation class riotous carry on laid up MO (15)
- 5 Add to area between buildings (8)
- 6 Amniotic fluid not in 2 is part of this make-up (6)
- 7 Inject intravenously in menial building (8)
- 15 We hear you are in charge of current identification of stone constituent (4,4)
- 16 Patient gave up (8)
- 17 Find out about rare kind of light (8)
- 19 Drill discipline (6)
- 21 Good, Round Table rule out trouble (3,3)
- 22 Checks borders (6)

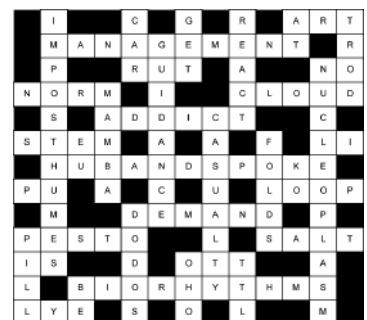
### Across

- 8 Paella King George made for malnutrition problem (8)
- 9 Put off revision of postulate about bone (6)
- 10 Strength of very many difficult clues (6)
- 11 Complained about first class list lacking a neurotransmitter (8)
- 12 Opposition leader presses about drink (8)
- 13 Left in the lurch intentionally, poor kid (6)
- 14 Measurements to find out if run durations met potential? (10,5)
- 18 Avoids failures (6)
- 20 Varied AutoAnalyzer component (8)
- 23 Phage not possibly an infectious agent? (8)
- 24 Breaking metatarsus sets off emotional shock (6)
- 25 Sober one fermented sugar (6)
- 26 Participants in reaction about moles (8)

### Down

- 1 Removes problem of French listening devices (6)
- 2 Designation of an 8-bit computer and a debit card (8)
- 3 Unhappy messenger men leave for exit (6)

## Solution to the Colley Christmas Crossword



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## Senior Scientific Officer - Biochemistry Permanent, Full Time

A vacancy has arisen for a Senior Scientific Officer in Endolab within the Specialist Biochemistry cluster at Canterbury Health Laboratories, Christchurch, New Zealand.

This reference laboratory provides a clinical service for both hospital and community health laboratories in New Zealand using a range of manual, in-house and automated immunoassay techniques. The laboratory also has a close working relationship with other research and development medical laboratories and clinical researchers in Christchurch.

This person will provide scientific leadership for a team of laboratory staff who strive to introduce improved and original methods for measuring existing and newly described hormones and related substances and to investigate their clinical application and to translate these findings into a diagnostic service.

Analytical experience using LC/MS technologies or other advanced techniques would be an advantage.

The successful candidate will have a PhD and be registered (or able to gain registration) with the NZ Medical Sciences Council.

The hours of work are Monday to Friday (0800 – 1700).

The position description is available on [www.careers.cdhb.govt.nz](http://www.careers.cdhb.govt.nz)

Please apply online or to discuss this role in more detail, contact Peter Skidmore, Section Head Endolab on 64 3 3640848 or email [peter.skidmore@cdhb.govt.nz](mailto:peter.skidmore@cdhb.govt.nz)

Location: Christchurch, New Zealand

**Closing date: 27th January 2012**

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### To advertise your vacancy contact:

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**Deadline: 26th of the month prior to the month of publication**

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