

ACBNews

The Association for Clinical Biochemistry | Issue 586 | February 2012

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ACB News

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*Front cover: Andrew Hartland and
Sud Ramachandran report on their
visit to Shenzhen*



Focus
Association for Clinical Biochemistry
National Meeting
Liverpool 2012



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

focus on the patient
www.focus-acb.org.uk

What's Happening in the World

Joe O'Meara, Government Affairs Officer

During 2012 the Association has three important strands of activity to increase our influence and build awareness of our profession and its importance:

- ◆ The Labs Are Vital Champions Programme
- ◆ Events for the National Year of Pathology
- ◆ Sponsorship of the "Voice of Young Science" activities of "Sense About Science"

Champions Programme

Labs Are Vital (LRV) is focusing on informing, educating and influencing Health Service commissioners in the context of laboratory medicine services during 2012. We aim to achieve this through "champions" nominated by the LRV sponsor organisations. The ACB is identifying people with a depth of knowledge and experience in delivering high quality services and eager to engage with commissioners and managers to share that experience through the regional committees.

A programme of activities together with support material and training for the champions is being developed and a major launch event is planned for late Spring.

National Pathology Year

The year was launched with an event at the Royal College of Pathologists on January 12th. Suzy Lishman, College Vice President, in her opening address, recognised the valuable contributions of the ACB and its members towards the success of the "National Pathology Weeks" and welcomed our anticipated major contribution to National Pathology Year.

I am endeavouring to keep track of events planned by the ACB and will put information on the ACB website so that we can all see what is planned from an early stage and volunteer and/or co-ordinate between projects. I hope anyone planning an event, even if only at a very tentative stage at the moment, will send me some basic details including Event Name, Date(s) it is taking place, Brief Description, Location, Main Contact Name, Telephone Number, Mobile

Number, Email Address, Hospital/Trust, ACB Region, Web link to any support material you are prepared to share, and 'Are you looking for volunteers to help? (Yes or No)'.
 If your project is at a more advanced stage it would be best to register on the college website (link) and just let me know so that I can get the details from there. To date I have only heard from two of our members about three planned events and I am sure there must be more in the pipeline. By making the information available at an early stage, others will be able to get some ideas and inspiration for events of their own or can put themselves forward if you are looking for volunteers to help with your event.

Sense About Science – Voice of Young Science

The ACB has an ongoing relationship and collaboration with the "Sense About Science" organisation, for example with the Making sense of screening and testing booklets. We have always been very supportive of their "Voice of Young Science" initiative (VoYS) which aims to give early career scientists an opportunity to express their views on scientific topics and controversies in a public arena. ACB Council has decided to sponsor VoYS during 2012 and encourage our early career members to participate actively. One way is to take part in a workshop to increase awareness of how to be involved with the media.

Our sponsorship guarantees us five places at such VoYS events during the year. The next event takes place on 23rd March 2012 at the University of Manchester. Details have already been circulated to trainee members. The information is also available at http://www.senseaboutscience.org/data/files/VoYS_workshop_Manchester_23March2012.pdf and anyone wishing to participate can apply direct to Victoria Murphy, noting their membership of the ACB at (vmurphy@senseaboutscience.org). Please let me know if you are applying for a place. ■

Early diagnosis of **Acute Kidney Injury (AKI)**

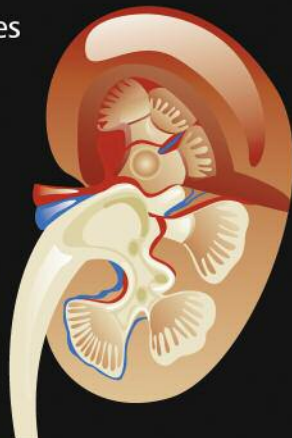
Neutrophil gelatinase-associated lipocalin (NGAL) provides an indication of AKI within two hours of an event.

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See us at the
ACB Spotlight Meeting on AKI
28 March 2012
Royal College of Pathologists,
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ACB Southern Region Spring Scientific Meeting and Annual General Meeting

From Humans to Steroids and Back. Clinical, Analytical and Genetic Aspects

A Festschrift for Dr John Honour to be held on 27th March 2012

The Neurosciences Building

National Hospital for Neurology & Neurosurgery

33 Queen Square, London WC1N 3BG

- 09:30-10:00 Registration & Coffee
09:55 Introduction
10:00-10:30 Congenital Adrenal Hyperplasia; An Evolving Role for the Steroid Biochemist
Professor Peter Hindmarsh, GOSH, London
10:30-11:00 Urinary Steroidobolomics and Disorders of Adrenal Corticosteroid
Professor Paul Stewart, Birmingham
11:00-11:30 Alternative Pathways to Partial Androgen Insensitivity
Dr Gerry Conway, UCLH, London
11:30-12:00 Agile; The Equipment Behind the Science
12:00-13:30 Lunch plus Southern Region ACB AGM
13:30-14:00 Analysis of Steroids in a Service Laboratory
Dr Brian Keevil, Wythenshawe, Manchester
14:00-14:30 Rapid Point of Care Tests for Small Molecules Such as Cortisol
Professor Colin Self, Newcastle
14:30-15:00 Dehydroepiandrosterone; An Interesting Substance
Dr Mike Wheeler, Exeter
15:00-15:30 Androgens and The Skin
Dr Julian Barth, Leeds
15:30-15:45 Tea
15:45-16:15 Adrenal Surgery for Biochemists
Mr Tom Kurzawinski, UCLH, London
16:15-16:45 Diagnosing Disorders of Sexual Development - From FISH to Chips and Beyond
Professor John Acherman, ICH, London
16:45-17:00 A Personal Appreciation of John Honour
Dr Gill Rumsby, UCLH, London
17:00 Dr John Honour, followed by refreshments

The meeting includes refreshments and lunch and will be accredited for 5 CPD points.
Cost of meeting: £25 for ACB Members, £15 retired ACB Members, £40 non-Members.

Maps and travel details may be found at:

<http://www.uclh.nhs.uk/OurServices/OurHospitals/NHNN/Pages/Home.aspx>

Further details from: Dr John Land Tel: 020 3448 4768 Email: john.land@uclh.nhs.uk

ACS Assessors Sought

The ACB is currently canvassing for new assessors on behalf of ACS.

You should be of appropriate professional standing, normally at AfC band 8c or above and have been registered for at least six years with HPC as a Clinical Scientist. You should preferably also be involved in the formal training of clinical scientists.

If you are interested in being considered for this role, wish to know more about the commitment required and meet the basic requirements above please send Mike Thomas an email at: president@acb.org.uk ■

Have Your Say on Annals Reviews

Would you like to contribute to the content of the Annals of Clinical Biochemistry? The Clinical Sciences Reviews Committee (CSRC) is seeking new membership. CSRC is a standing committee of the ACB Scientific Committee, with a specific remit to promote a wider understanding of the practice of our profession by commissioning topical and relevant articles. Reviews are generally invited by the committee from leading national and international experts.

The Committee works with the authors defining the scope and style of the article, peer reviewing and formatting the final manuscript and submits these to the journal. Articles are usually, but not exclusively, published in the Annals of Clinical Biochemistry as either 'Comments', 'Personal Views' or 'Reviews'.

Ordinary membership is for a term of three years. The Committee meets three times a year in London and most of the work occurs via email.

Anyone interested should contact either: Michelle Young, CSRC Secretary, (michelleyoung5@nhs.net) or David Gaze, Chair, (david.gaze@stgeorges.nhs.uk). ■

Sudoku

This month's puzzle

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

Last month's solution

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

Coming Next Month

As we build up to Focus next month we will look at some of the good things that are coming at Focus in Liverpool. ■



Deacon's Challenge

No 129 - Answer

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.

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. However, we are now dealing with concentrations and times rather than rates so the integrated form of the Michaelis-Menten equation is used (see Wagner GW, *J Pharmokinetics Biopharmaceutics* 1973, **1(Part 2)**: 103-121)

$$V_{max} \cdot t = C_0 - C_t + K_m \ln(C_0/C_t)$$

Where	C_0	=	initial concentration	=	30 mg/L
	C_t	=	concentration at time t	=	10 mg/L
	K_m	=	Michaelis-Menten constant	=	5.0 mg/L
	V_{max}	=	maximal velocity	=	312 mg/24 h/total vol

Note that the units of V_{max} determined from the Mullen nomogram are mg/24 h/total volume of distribution and need to be converted to mg/h/L since plasma drug concentrations are mg/L and we need to calculate time in hours. Therefore the V_{max} needs to be divided by 24 and the total volume of distribution:

$$\begin{aligned} \text{Total volume of distribution (V}_d\text{)} &= \text{Body weight (Kg)} \times \text{Vol distribution (L/Kg)} \\ &= 75 \times 0.65 = 48.75 \text{ L} \end{aligned}$$

$$V_{max} \text{ (mg/h/L)} = \frac{V_{max} \text{ (mg/24 h/total V}_d\text{)}}{24 \times \text{Total V}_d}$$

$$= \frac{312}{24 \times 48.75} = 0.267 \text{ mg/h/L}$$

Substitute these values into the integrated Michaelis-Menten equation and solve for t :

$$0.267 t = 30 - 10 + 5.0 \ln(30/10)$$

$$0.267 t = 20 + 5.0 \ln 3$$

$$0.267 t = 20 + (5.0 \times 1.10)$$

$$0.267 t = 20 + 5.5 = 25.5$$

$$t = \frac{25.5}{0.267} = 96 \text{ h (to 2 sig figs)}$$

Therefore it will take 4 days for the plasma phenytoin to fall to 10 mg/L. ■

Question 130

Haemochromatosis, a cause of abnormal liver function tests (LFTs), has a UK allele frequency of 0.07. Iron overload due to haemochromatosis can be demonstrated in 80% of men aged over 40, using a raised serum transferrin saturation. A commoner cause of abnormal LFTs is non-alcoholic fatty liver disease (NAFLD), with a reported prevalence of 5%. Unfortunately, raised TSat has also been reported in 7.4% of patients with abnormal LFTs due to NAFLD (and there is no association between NAFLD and haemochromatosis).

Assuming that there are no other causes of raised TSat, in what percentage of male patients over 40 with abnormal LFTs will a raised TSat indicate haemochromatosis? State any assumptions made.

FRCPath, Spring 2011

Microbiology in the News

Dr Zoie Aiken & Michelle Lister

Anyone for Oysters?

A recent study conducted by the Centre for Environment, Fisheries and Aquaculture Science found that 76% of oysters harboured Norovirus (winter vomiting virus). More than 800 samples were examined from 39 different oyster harvesting areas between 2009 and 2011. It is difficult to interpret these findings as an acceptable level of norovirus in shellfish has not yet been defined. High levels of contaminants can build up within these filter-feeding organisms, and the industry attempt to reduce the microbiological burden by re-layering (moving shellfish to clean areas) and depuration (shellfish are placed in tanks of UV-treated, re-circulating water). Norovirus is spread predominantly from person-to-person, but food remains an important fomite. Symptoms include projectile vomiting and diarrhoea, but it is generally a self-limiting infection and recovery occurs after 2-3 days.

<http://www.independent.co.uk/life-style/health-and-families/health-news/norovirus-found-in-oysters-6269714.html>

<http://www.food.gov.uk/news/newsarchive/2011/nov/norovirus>

Faecal Transplantation

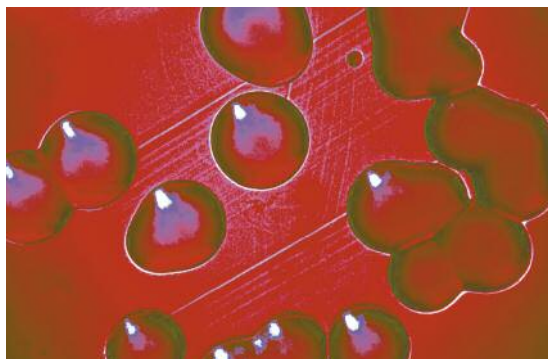
An Infectious Disease Consultant from Gartnavel General Hospital, Glasgow has become the first UK doctor to use faecal transplantation to treat *C. difficile* infection. Faecal matter from a donor was given to the patient via a nasogastric tube; usually the opposite end of the gastrointestinal tract is used to administer the bowel microflora into a recipient. The theory behind the treatment is that the 'good bacteria' from the donor will out-compete *C. difficile*, resulting in a cure to the diarrhoea and other symptoms it causes. Although this treatment sounds pretty disgusting, the success rate is nearing 90% and the procedure is only used after traditional antibiotic therapy has failed.

<http://www.bbc.co.uk/news/health-15113440>

Are Antibiotics Making us Fat?

Researchers in the United States are investigating whether altering our bacterial microflora by using antibiotics, can make us put on weight. One bacterium, *Helicobacter pylori* has received the most interest. This microbe can inhabit the stomach and promote the development of peptic ulcers and cancer. Therefore, it seems logical to treat infected patients with antibiotics in order to eliminate the pathogen from the body. However, not everybody harbouring *H. pylori* develops peptic ulcers, and patients who have been treated for *H. pylori* infection are at greater risk of developing gastric reflux and other oesophageal diseases. Additionally, patients without *H. pylori* have higher circulating levels of a 'hunger hormone' known as ghrelin; levels of this hormone normally drop after eating as a signal to stop. So it has been suggested that a change in the microbiota of these patients could be causing them to over eat. The microbiota of obese subjects has also been studied and compared to control subjects with a healthy weight. The range of species identified in the two patient groups were found to be significantly different, which perhaps suggests that changing the microbiota of individuals with a healthy weight by the use of antibiotics, may be the first step towards developing obesity.

http://www.nytimes.com/2011/11/01/health/scientist-examines-possible-link-between-antibiotics-and-obesity.html?_r=1&ref=bacteria



Looking East for Pathology Direction

Jonathan Berg, Editor

Introduction

Since Lord Carter's reviews of Pathology, SHAs in England have been taking forward projects to implement change focused on saving 20% of the pathology budget. Some SHA-wide pathology projects have recently faltered but the East SHA initiative looks like it will move to completion. The strategy that has been developed is being portrayed as a national model for England on how to commission pathology services. The project team responsible have now become the strategic team for the new Midlands and East SHA. Studying their methods and ways of working is helpful both in the pathology arena and also more widely on other NHS services.

NHS East of England

The strategic group undertaking the pathology transformation project is headed up by Dr Stephen Dunn, Director of Strategy Provider Development. Stephen is closely linked to the concept of Foundation Trusts. Over the last few years he has worked in the East of England to develop rigorous foundation trust assessments and has also overseen externalisation of PCT providers. His team also took forward the tendering for Hinchingsbrooke Healthcare NHS Trust which was awarded to Circle. His 2010 book: "The Economics of John Kenneth Galbraith: Introduction, Persuasion, and Rehabilitation", elicited the following review: *'Stephen Dunn has produced a timely, insightful and valuable introduction to the economic thinking of J. K. Galbraith. It deserves to be widely read and it will inform debate in these interesting times.'*

Alan Milburn MP

Others with key roles in taking things forward include Andrew MacPherson, Strategic Projects Director, whose past projects include rail privatisation and a close interest in customer

service. Dr Hemal Desai is the Clinical Advisor and is best known within Pathology as an advisor to Dr Ian Barnes at the Department of Health. Besides his work on pathology transformation in East SHA he is also a practising GP in urgent care in London.

Pathology Services Project Boards tasks include:

- ◆ Reviewing commissioning of community Pathology services.
- ◆ Reviewing provider networks and encouraging outline business cases for change.
- ◆ Developing and implementing effective strategies to involve stakeholders.

East SHA Pathology Transformation Plans

The overview is clearly a move to Hub and Spoke pathology delivery and the mechanism is an intra-NHS tendering process with a clearly defined number of hubs for secondary care Pathology. Existing Trusts in East of England collaborated with each other to submit bids to become a GP hub. Trusts are able to include services from the independent sector if they feel it can improve the quality of care they can offer to GP Pathology.

The process includes a pre-qualification questionnaire and following this a submission in the form of an invitation to participate in dialogue stage was issued. The first of the dialogue meetings took place in August 2011. The timeline then shows a key milestone of an invitation to tender date 24th January 2012 with a submission date of 14th February 2012. A contract award is intended to be made sometime after April 2012.

Stephen Dunn was a keynote speaker at "Innovating for Excellence" on 23rd November 2011 at Loughborough University. Stephen spoke of a "lack of tolerance" to those who were not taking forward transformation

Key Programme Milestones	Timeline – Week No.
Invitation to participate in dialogue (ITPD) issued	0
Dialogue meetings	2
Period of consideration	3-4
2nd dialogue meetings	6
ITPD submission deadline	7
ITPD Evaluation	15-18
Confirmation of bidders recommended to proceed to Invitation to Tender (ITT)	25
ITT Issued	26
ITT Submission deadline	29
ITT Evaluation	29-32
FBC preparation and approvals	37
Commissioning Contract Award and Signature	To be confirmed
Service Commencement	To be confirmed

projects when there was evidence that they should be. He cited Pathology restructuring as a major area to be driven forward.

Key Points

- ◆ The East of England Project Team has a clear priority for Pathology transformation. There has been a major investment with management review followed by project initiation documents moving on though an outline business cases to a full tender process.
- ◆ The pathology transformation only looks at provision of the service to GPs/Community pathology. The process taken forward is an intra-NHS restructuring. Any Trust in the East SHA was able to put in a proposal to be a hub but there was strong encouragement to collaborate with others in the region and the independent sector as subcontractors – if “they consider this is appropriate and will strengthen their proposals”.
- ◆ The East SHA exhibits strong and firm leadership from the Transforming Pathology Services Board. The outline business case makes it clear that the Strategic Project Team will be negotiating the contracts with hub providers on behalf of the commissioners.
- ◆ The outline business case was approved with their option of 3 to 4 hubs to

undertake GP/Community work. The outline business case is seen as a restructuring to a smaller number of hubs as an interim solution prior to a “move to deregulated market provision in the longer term”.

- ◆ There were 6 bidders considered at the Invitation to Dialogue stage in total who included all current pathology providers and a number of the bids involved the private sector. During the dialogue stage it was indicated that the collaborative bids may change membership.

Wider Significance of this Process

An interesting part of this strategy is that the initial emphasis is portrayed to be on the primary care pathology work. In the current model this must have required agreement with PCTs that the SHA takes over the process of procuring pathology services on behalf of primary care. Alliances formed between current NHS pathology laboratories are presented at a pre-tendering stage and if found not to be acceptable are either rejected or potential bids are told to go back and come up with something more acceptable. So, while the appearance is of the tendering for primary care the reality is that the whole of the pathology delivery is being tested through this process.

So, the East of England model is now in the final stage of intra-NHS tendering but the real success or otherwise of the approach will only be seen in the medium and longer term. In October, NHS East of England SHA joined with the SHAs in West and East Midlands, to form the new NHS Midlands and East. Dr Stephen Dunn has been appointed Director of Policy and Strategy and his team are undertaking a review of the progress in pathology transformation projects across the new SHA.

The East SHA strategy for pathology change includes a strong strategic projects team. One key element of their change programme is a

clear commitment to highly professional communication and this can be reviewed at their website (www.strategicprojectseoe.co.uk). The team are currently compiling a pathology services commissioning framework to support the Department of Health's National Pathology programme. They say on their website that "this is in the form of a toolkit, designed to support commissioners to commission high quality, affordable pathology services which demonstrate value for money for GPs and other clinical practitioners (the service users) and their patients". ■

THERAPEUTIC DRUG MONITORING



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* GLP GCP COMPLIANT *

* EQA SCHEME MEMBERS *

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The NHS Constitution and “Whistle-blowing”

Alan Penny, FCS Case Registrar

Report of Department of Health Consultation: September 2011; Guidance for FCS Members & Representatives

In October 2010 the Government initiated a public consultation on proposals to clarify and strengthen the position of those who make public interest disclosures, sometimes referred to, incorrectly, as whistle-blowers in the NHS. The proposals which follow on from some of the serious healthcare failures over the past decade or so, expect staff of all standings to raise any genuine concern they may have about a risk, malpractice or wrong-doing at work, (such as a risk to patient safety, fraud or breaches of patient confidentiality) which may affect patients, the public, other staff or the organisation itself at the earliest reasonable opportunity. The HPC’s “Standards of conduct, performance and ethics” indeed make it a professional duty of registrants to raise concerns about a situation “that puts a service user in danger” to “a senior colleague or another appropriate person”.

Protection Against Detriment is Not Freedom to Say Anything!

The consultation report is now published and can be downloaded in full at: http://www.dh.gov.uk/en/Consultations/Responsetoconsultations/DH_130551 The Department of Health has taken up many of the comments and proposals submitted by contributors, including FCS and other unions. The next step is to amend the NHS Constitution and Handbook through Staff Council along the lines proposed in the consultation report, which should be read fully.

The proposals bring the NHS Constitution in line with the Public Interest Disclosure Act 1998 (PIDA) and reduces the likelihood of differential treatment between Trusts. It does not give NHS staff complete freedom to make public condemnation of local or national policies such as proposed closures, nor to criticise individuals for unpopular decisions.

Internet Forums Comments are Not Wise

“PIDA”, which amended the Employment Rights Act 1996, is part of wider employment rights legislation. It provides legal protection against detriment in the work place to all workers in England and Wales who act in good faith and in the public interest by disclosing concerns, providing they follow the procedure set out in PIDA. The law therefore applies to all employees and workers including contractors (but not volunteers) working in the NHS. Concerns can be raised (in England) with the NHS funded organisation in which the individual works, to a legal adviser, a Minister of the Crown, or a person prescribed under PIDA, which includes the Care Quality Commission (CQC) or, in the case of Foundation Trusts, Monitor. The CQC in December 2011 published its own guidance for healthcare staff. This can be downloaded from: http://www.cqc.org.uk/sites/default/files/media/documents/20111214_whistle_blowing_quick_guide_final.pdf

Members in Scotland, Wales or Northern Ireland should check who would be the equivalents under their administrations. Members must be fully aware that the legal protection of PIDA only applies if they follow the correct procedures as laid down in PIDA and local policies (all Trusts will have one). In summary, they are protected against victimisation (defined as detrimental treatment by your employer or colleagues as a result exercising a legal right) when they

report internally but must be very careful if they contemplate going public (outside NHS). The media and internet forums are definitely not recommended. Even if anonymity is intended and assumed this is not guaranteed and you have no editorial control that the integrity or context of your content is preserved. The civil laws on liable and slander, Trust policies on bringing the employer into disrepute and HPC/GMC standards of conduct still apply to these situations and no legal protection applies.

The Consultation Report identifies a group called "appropriate persons" from whom staff may obtain advice and guidance before making a complaint. The Government has accepted comments from TUs to include us within this group which now includes representatives of professional bodies, regulatory bodies, trades unions, legal advisors, or a confidential telephone helpline currently funded by DoH and provided by Public Concern at Work (Tel: 020 7404 6609). Others such as the Citizens Advice Bureau and MPs may be allowed but are not specified. Staff would be ill advised to take any action without consulting first. Proof of the suspected wrong-doing is not required but the whistle-blower must be acting in good faith and the public interest, as opposed to personal interest, including discrimination as these should be tackled via the grievance procedure. The complaint should be made initially in confidence and preferably in writing to facilitate investigation.

Moving Up the Line Appropriately

There is a hierarchy of people to whom complaints and concerns may appropriately be reported depending on the circumstances and seriousness of the wrong-doing:

- ◆ Your line manager or lead clinician
- ◆ Your Head of Department
- ◆ Your Clinical Director
- ◆ The Designated Officer within the Trust (this is the post responsible for medical staff revalidation, usually the Medical Director)
- ◆ Trust CEO

- ◆ Trust non-Executive Director
- ◆ Minister at DoH, Care Quality Commission or Monitor

If the first person does not properly address the issue or take adequate action then the member of staff should go higher up the line but not outside of it. Those raising issues do not have a right to be informed personally about the outcome.

Advice is given on wider disclosure under specified circumstances as a last resort, but this should not be undertaken without guidance and may be best raised by an organisation such as your professional body or trade union rather than by you as an individual.

If you have a concern regarding a professional in another part of the NHS, or even outside of it, then you need to get advice on who to raise it with. The principle would again be through the clinical management structure. If your service is a customer then your own clinical lead would be appropriate. If the matter is outside of your normal interactions then the PCT might be appropriate. Each such case merits individual consideration which his why it is wise to seek advice.

Protected Disclosure Not Whistle-Blowing

In certain circumstances wider disclosures to bodies or persons other than your employer or a Minister of the Crown may also be protected by PIDA. A number of additional tests, aside from reasonable belief and good faith, will apply to assess whether such a disclosure is a "protected disclosure". Those additional tests will vary from case to case and may include consideration of the following factors:

- ◆ The identity of the body/person to whom the disclosure is made (generally disclosures to the media are unlikely to be covered), and the seriousness of the alleged breach and
- ◆ whether it is "an exceptionally serious concern";
- ◆ there is a risk that evidence could be destroyed or concealed if the disclosure is

made to the employer or another prescribed person;

- ◆ the disclosure amounts to a breach of confidence with the employer;
- ◆ the matter has already been raised;
- ◆ there is a good reason to believe that the individual will be the subject of a detriment by their employer if the matter were raised internally or with another prescribed person; and
- ◆ disclosure was reasonable given the circumstances.

Staff considering such a disclosure are advised to take advice from the helpline, their trade union or their professional regulatory body before taking this step."

If any member of staff does suffer detriment of any kind as a result of making a valid disclosure redress is first using the local employer's the grievance procedure or in the case of dismissal via the Employment Tribunal system. If a link can be demonstrated then dismissal is automatically unfair and awards will be uncapped. Any member believing they

are in this situation should contact their FCS representative.

Use of the term "whistle-blowing" is an unfortunate yet very common misconception. What is really meant is a protected disclosure within the NHS structure as defined above. However in the normal context of whistle-blowing, i.e. reporting issues into the public domain there is unlikely to be any protection.

All members must be fully aware of the strict code of professional conduct that they agreed to accept upon registration. HPC and GMC expect us to act professionally and abide by the code at all times not just while at work.

If an FCS representative is contacted by a member for advice on disclosure please advise them carefully and seek help if necessary.

- ◆ From 1st January 2012 a new, confidential and independent advice helpline has been launched, provided by the Royal Mencap Society. It is available weekdays between 08:00 and 18:00 on 0800 0724 725. This is also available to employers and managers for advice on best practice. ■



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Sex in the City

Joe Bailey, Imperial College, London

The ACB Southern Region Winter Meeting, 'Sex, NETs and Dynamic Function Tests', was held on 25th November at Charing Cross Hospital in West London

The morning session dealt with the 'sex' part of the title. Starting proceedings was Professor Waljit Dhillon, Consultant Endocrinologist at Imperial College Healthcare NHS Trust, who described his research into kisspeptin. Kisspeptin is so called because of its discovery in the famous chocolate-making town of Hershey, Pennsylvania. It is a peptide hormone expressed in the hypothalamus, gonads and placenta. It stimulates the hypothalamic release of gonadotrophin-releasing hormone via the GPR54 receptor. Mice or humans lacking kisspeptin or its receptor fail to undergo puberty and are infertile. Prof Dhillon's group has shown that infusion of the hormone stimulates gonadotrophin secretion in healthy human volunteers. Furthermore, twice-weekly kisspeptin infusions in women with hypothalamic amenorrhoea bring about a partially-sustained release of luteinising hormone. Research is ongoing into the potential utility of kisspeptin in infertility treatment.

Anti-Müllerian Hormone

Next, Rebecca Leyland, Senior Clinical Scientist at the Royal Free Hampstead NHS Trust, gave an overview of the routine use of Anti-Müllerian Hormone (AMH) measurement. AMH is a glycoprotein which, in the developing male embryo, induces the regression of the Müllerian ducts and thus regulates male sex differentiation.

In females, AMH is produced by the granulosa cells of growing ovarian follicles. Levels of the hormone peak at around 20 years

of age and gradually decline until the menopause. AMH has four main areas of use in females: assessing ovarian reserve, predicting the response to IVF, investigating possible PCOS and as a potential tumour marker of ovarian cancer. The circulating concentration of AMH reflects the growing follicle population and therefore has a strong correlation with antral follicle count. A decline in ovarian reserve can be detected earlier using AMH levels, as they decline before other markers.

Current assays for AMH are manual plate-based ELISAs. While a NEQAS scheme for the hormone is now available, lab measurement suffers from the lack of an international standard, no age-related reference ranges and no consensus on concentration units.

Semen Analysis and the New WHO Recommendations

Dr Kevin Lindsay, Consultant Clinical Scientist in Andrology at Imperial, discussed the new recommendations from the World Health Organisation on the analysis of semen. Among the changes from previous practice is the recommendation that semen volume now be determined by weight. Pipetting to assess volume means that up to 40% of the semen can be lost, whereas weighing reduces this error to only around 1%. However, this requires pre-weighed pots, which are difficult to procure!

Defining a normal sperm in the Andrology lab is also difficult. The proficiency of labs at doing this under EQA is assessed using virtual slides. The audience was shown a collection of such slides and the variation in responses illustrated the scale of the task!

Gonadotrophinoma

Rounding off the morning session, Dr Monica Nijher, Wellcome Research Fellow at Imperial, described a case of a female patient with irregular periods, galactorrhoea and frontal



hair loss. Gonadotrophins and prolactin were raised on initial lab analysis, while an MRI scan showed a pituitary macroadenoma to be compressing the optic chiasm. Histology after transsphenoidal surgery revealed this to be an FSH-secreting adenoma. Following glucocorticoid therapy for post-operative hypopituitarism, the patient was well and trying to become pregnant a year later.

Such gonadotrophinomas are rare and mimic premature ovarian failure in women. In men, signs of testicular enlargement may be present and there are also a few cases of gonadotrophinomas leading to precocious puberty in children. Measurement of basal intact gonadotrophins has limited use in pre-operative identification of the tumour type.

Gut Hormones and Neuroendocrine Tumours (NETs)

After lunch, the focus moved on to NETs and the use of gut hormones to diagnose and monitor them. Such hormones include insulin,

gastrin, glucagon, chromogranins and the new marker, cocaine and amphetamine regulated transcription protein (CART).

Dr Tricia Tan (Consultant in Metabolic Medicine and Endocrinology) described the classification of NETs. The gastroenteropancreatic NETs (GEP-NETs) are the largest group, comprising mid-gut NETs (2/3) and pancreatic NETs (1/3). Insulinomas are the most common type of functioning pancreatic NET and can be diagnosed by the demonstration of hypoglycaemia, with inappropriately raised insulin and C-peptide, after a 72 hour fast. Gastrinoma is the second most common type of pancreatic NET, characterised by inappropriately high gastrin levels and excessive acid production. Gut hormone profiles are valuable in the diagnosis, prognosis and follow-up of these tumours.

Following the clinical and biochemical diagnosis of a pancreatic NET, localisation of the tumour is required. This can be done using CT or MRI scanning, endoscopic ultrasound, or octreotide scanning. Confirmation can be

achieved with arterial stimulation/venous sampling (ASVS). In this technique, arterial calcium infusion stimulates an insulinoma to release insulin into the venous system, which can be measured to allow localisation of the tumour to a particular arterial territory of the pancreas.

Chromogranins

The chromogranins are the most commonly assayed gut hormones in the detection of functioning NETs and Dr Radha Ramachandran, SpR at Imperial, talked specifically about their use. The chromogranins are the major components of the secretory granules of most neuroendocrine cells and serve as general markers of NETs.

Sensitivity of Chromogranin A (CgA) assays is low in early disease and so the hormone must not be used as a screening marker for NETs. For the diagnosis of a NET, measurement of CgA should only be carried out with an image-positive tumour or where there is strong suspicion.

In assessing prognosis, CgA levels correlate with tumour load, progression and response to therapy. The five year survival rate in NET patients with raised CgA levels at diagnosis is lower than in patients with normal levels.

CgA immunoassays suffer from the lack of a reference standard and reference method. While all assays are very similar in diagnostic accuracy, they are not directly comparable as they all measure different epitopes on the CgA molecule. Measuring chromogranin B alongside CgA improves diagnostic sensitivity and specificity.

Cocaine and Amphetamine Regulated Transcript (CART)

Dr Kevin Murphy (Reader in Endocrinology and Metabolism) next spoke about the use of CART. First discovered in studies of the effects of cocaine and amphetamine on the rat brain, CART is a 116 amino acid peptide expressed in the hypothalamus, pituitary, adrenals, pancreas and GI tract. While its exact function remains unknown, CART has been shown to be



upregulated in NETs. When measured alongside CgA, it is an excellent marker of disease activity, with very high sensitivity and specificity for active disease above a cut-off of 80 pmol/L.

An example of the use of CART is in the assessment of the activity of pheochromocytoma, a NET of the adrenal medulla. Previously, the classification of the disease as malignant relied on the presence of distant metastases. However, it is now known that expression of both CART and CgA in chromaffin cells of the adrenal medulla is higher in metastatic disease than in non-metastatic disease.

Ongoing work is focusing on the potential utility of CART in predicting NET behaviour and monitoring response to therapy.

NET Case Study

Dr Sarah Darch, Clinical Scientist at Imperial, took us into the afternoon tea break with a case study highlighting the clinical utility of gut hormone measurement. A 28-year-old female with recurrent episodes of peptic ulcers was investigated for a gastrinoma and diagnosed with Multiple Endocrine Neoplasia (MEN) Type 1. She developed symptoms consistent with an insulinoma. ASVS with calcium stimulation revealed two gastrinomas and one insulinoma. These tumours were resected.

After several years of relatively good health, levels of CgA and gastrin were seen to rise during a successful twin pregnancy. A CT scan after delivery showed a 5 cm pancreatic mass.

At a pre-operative review six months later, symptoms of a recurrent gastrinoma were present, while CART and CgA levels had increased by 100 fold and 10 fold respectively. The levels of these hormones reflected the disease course, with an initial decrease following debulking surgery and chemotherapy. However, the patient became resistant to chemotherapy, CART and CgA again rose (suggesting progression of disease) and the patient passed away.

Interactive Endocrine Cases

The packed schedule was concluded with an interactive case session presented by Dr Amir Sam of Imperial. Dr Sam used several unusual endocrine cases to illustrate some salient points, including the use of serum phosphate to determine whether or not thyroidectomy patients can be discharged early. In normal individuals, serum phosphate levels are lower on waking in the morning than before bed the previous evening. Thyroidectomy patients following this normal pattern on the first morning after surgery can be discharged as the risk of surgery-induced hypocalcaemia developing is deemed low. However, patients with morning phosphate levels higher than the previous evening are possibly hypoparathyroid, as parathyroid hormone (PTH) normally inhibits the renal reabsorption of phosphate, and risk developing hypocalcaemia. Measuring serum phosphate is a quicker and cheaper way of assessing this risk than PTH measurement. ■

Rethinking Drug Innovation with the Old and New Worlds

Dr Andrew Hartland & Dr Sud Ramachandran, West Midlands

A Report on the 9th Annual Congress of International Drug Discovery and Technology held in Shenzhen, China, November 3rd-6th 2011

The theme this year was “Rethinking drug innovations in the green eco era” and this conference (www.iddst.com/iddst2011/) was attended by the leading lights of Industry, University researchers and practising clinicians. Three Nobel Prize Laureates had accepted invitations to discuss their past, present and future work. There were 20,000 delegates who had registered making this a significant international event. On the surface it was an unusual meeting for two Chemical Pathologists to be invited to actively participate. We were asked to discuss our experience, views and research on drugs used in diabetes, dyslipidaemia and weight management.

Messages from the Meeting

The meeting opened with a high. Thomas Steitz from Yale University (Nobel Prize Laureate 2009) spoke about binding two antibiotics to create a designer antibiotic, less prone to resistance. He was followed by Ada Yonath from the Weizmann Institute in Tel Aviv (Nobel Prize Laureate 2009) who discussed the ways antibiotics inhibited protein synthesis at the ribosome levels, augmenting this with crystallographic illustrations. Avram Hershko from the Department of Biochemistry, Rappaport Faculty of Medicine, Jerusalem (Nobel Prize



Laureate 2004) described in detail the ubiquitin proteasome system.

Our session was titled “Diabetes and Other Metabolic Diseases” chaired by SR. Professor Zhang (Beijing Institute of Ophthalmology), updated us on her current research regarding the role of VEGF and diabetic retinopathy. This was followed by AH reviewing his experiences on weight reducing drugs, also looking into the future and outlining the requirements for

on-going development. Professor Jacobowicz (Universities of Virginia, Venezuela and Tel Aviv) presented data on the clock genes and their role in obesity; interestingly a high protein and high carbohydrate (incorporating both chocolates and donuts) breakfast led to significant weight loss. The last talk prior to the interval was by SR discussing changes in HDL-C and creatinine with fibrates. SR also described a novel group of patients demonstrating the paradoxical HDL-C decrease with fibrates. Professor Enslin (University of Missouri) spoke about the link between insulin resistance and the atherogenic lipoprotein phenotype focusing on NEFA. The last speaker was Professor Guo (Ohio State University) who described lipid pathways relating to SREBP-1. He then outlined a new agent designed and tested on cultured cells targeting SREBP-1 which may be of use in the treatment of glioblastomas. Overall the session was a mix of clinical and basic medical science and of a high standard befitting the quality of the meeting. Professor Zhang cordially invited both AH and SR to Beijing to meet her colleagues over dinner at the University of Beijing to discuss potential collaboration.

Messages from China

Shenzhen is a city in development with Industry as its theme and aspiration was everywhere. We tried to locate "old Shenzhen" to contrast old and new, without success. Shenzhen will undoubtedly be much changed even in the next five years. After the meeting we travelled to Beijing to experience its fascinating history and culture. We began by visiting the Olympic Park which was even more impressive when seen in person. Then we were transported back in time through Hutong, the old part of the city, on a bicycle rickshaw. We saw a China very different to that we anticipated. This was a China embracing capitalism and the modern world. There is no doubt that it is going to further itself as an economic and industrial superpower. We visited the Beijing Book Building, the largest book store in China and could not find an English translation of the thoughts of Chairman Mao; this request

resulted in significant mirth. This anecdote embodied modern China.

We were vegetarian for much of our visit (AH humouring the vegetarian SR) and this caused amusement and consternation in equal measure. Even asking for a fork at mealtime resulted in good natured laughter. The cars on the road tell one about the society as eruditely as anything else. In this, China could be Britain. German cars were everywhere. Even our tour guide said that German cars were considered a statement of quality. Mercedes, BMW, Audi, but above all Volkswagen were omnipresent. We saw only a lonely Landrover and a couple of Minis flying the Union Flag. The question has to be asked 'Why?'

The meeting provided clues as to why this was the case. We came across only one other delegate from the United Kingdom, a Gastroenterologist from East Anglia carrying out interesting research on statins and oesophageal cancer. This contrasted with the many delegates from the United States and other developed countries. Many were CEOs of manufacturing companies marketing their products. We did not see any British products. Was this the reason for the solitary Landrover and the brace of Minis? We have to investigate the reasons. Are we in Britain obsessed by internal restructure; is this at the expense of ignoring global opportunities? Within pathology we are entering another phase of network led restructure which once again focuses within the NHS organisation. At the same time the outside world have networked amongst themselves for mutual benefit. When we wake up, this period of opportunity may have passed and it may be a case of a solitary Landrover and the couple of Minis once again.

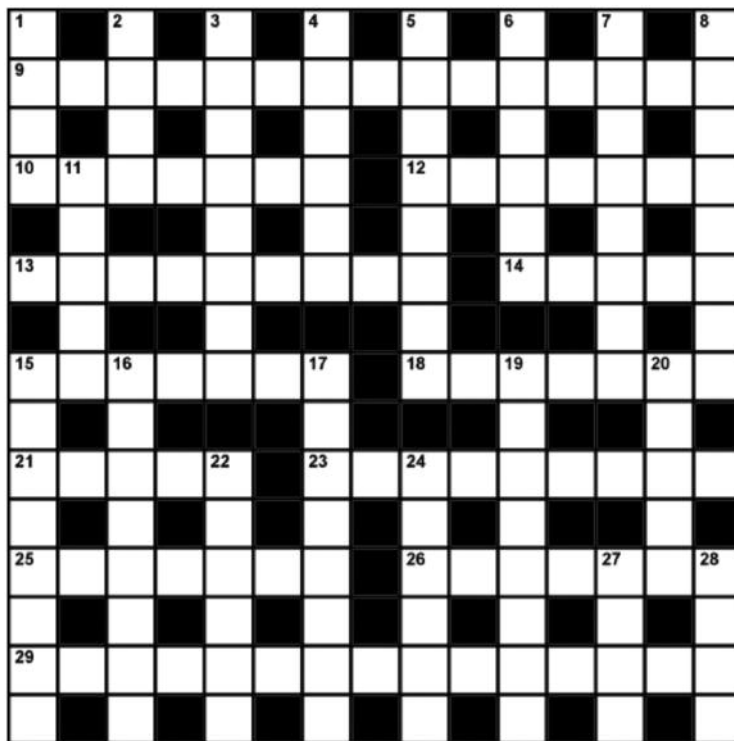
We have been invited to speak and chair at the World Diabetes Congress in Beijing next year. We do hope there will be more scientists and CEOs from the United Kingdom flying our flag. Many of you will receive invitations from China to participate and speak at meetings, but may not give it a second thought for various reasons. We urge you to consider it as you will have an experience like no other with a mix of old and new worlds. ■

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 around the 1st of each month.



- 6 Less fresh produce retails without number (6)
- 7 Larked about, overacted, lacked direction (8)
- 8 Nothing to secure starting handle for clinical instrument (8)
- 11 Circle over region of gas (5)
- 15 Gets together again about radicals (8)
- 16 Comment on a tenant upset about love (8)
- 17 Enzyme ingredients in meal starter broth (8)
- 19 Develops into nice addictive substance (8)
- 20 Description of strength that is double-edged, omitting resistance (5)
- 22 Exact requirement (6)
- 24 One of nine separators or one of the groups (6)
- 27 Warning symptom comprises two elements (4)
- 28 Sounds around Skye (4)

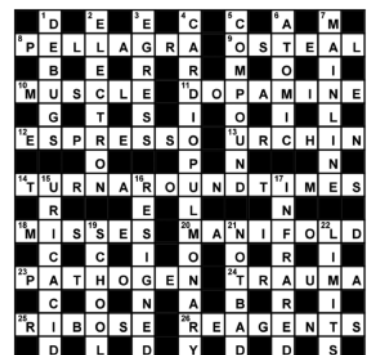
Across

- 9 Way for obtaining nourishment in meal tray involved accepting religious pamphlet (10,5)
- 10 Allot building in part exchange as a source of revenue (4,3)
- 12 PM's disease? (7)
- 13 Join? Decline! (9)
- 14 Proportion of lacerations doctor cleans out (5)
- 15 Enter silver amalgam as reaction constituent (7)
- 18 Denies one representation indefinitely (4,3)
- 21 Go and repair organ (5)
- 23 Abnormally truncated 15 (9)
- 25 Best sort of minicomputer - not any nicer! (7)
- 26 Reduction of share support (7)
- 29 Toe party line with gen about possible capacity for work (9,6)

Down

- 1 Fish or beef (4)
- 2 Execute while away (4)
- 3 Far less botched re-fractures for treatment (4-4)
- 4 A burden on one having a neurological condition (6)
- 5 They eat shoots and leaves; many study their displays (8)

Last month's solution



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