

ACBI West of the Shannon Meeting 2005

Rowland Reece, Principal Biochemist, St. Vincents University Hospital

A grand day out, as they say, as the hordes descended on the apparently sleepy town of Athlone on the 2nd September last for a meeting hosted by Ms. Niamh Cavanagh, Portiuncula Hospital, ably assisted by Dr. Helen Grimes and generously sponsored by Roche Diagnostics. This was to be Niamh's swansong (in meeting terms), as she has just recently retired, and, fittingly, it was indeed an excellent meeting.

The Radisson Hotel in Athlone, though technically east of the Shannon, was nevertheless a very good venue, accessible to all whether by car or by train and a large number of people attended (extra chairs had to be procured).

The morning session began with a well-titled journey through the vagaries of paediatric biochemistry from a clinician's perspective. Dr. Cook from the Paediatric department, Portiuncula, spoke about the tremendous difficulties faced by the caregivers and the Laboratory in getting results- and accurate ones at that- from the '26-weeker' up to the screaming tots, supported nicely with a couple of real cases and empathic photos.

2

Peter Auld from the Royal Victoria Hospital Belfast gave us a timely and extensive review of the current status of the B-type natriuretic peptides, focussing mainly on his own laboratory's experience with NT Pro-BNP in the diagnosis, prognosis and monitoring of heart failure. Examples of the evidence from a number of studies, including the CREST study in Northern Ireland, the PRIDE study and NICE guidelines show that BNP is definitely here to stay.

The last speaker before lunch was Helen Grimes, UCHG, who gave an excellent talk on Vitamin D. The incidence of deficiency and insufficiency appear to be increasing as our population profile changes. The difficulties of measurement and lack of agreement between various immunoassays was outlined and the recent growing interest in the genetics and the 'alternative' functions of this vitamin, particularly its role in cancer, means that all who attended were glad to be re-acquainted with vitamin D.

The afternoon session was concerned with C-reactive protein and vascular disease. Dr. Tom O'Malley, Consultant Geriatrician in Portiuncula, placed CRP in the inflammation hypothesis and outlined its role in the vascular syndromes, coronary heart disease and stroke. He gave some insight into the way CRP behaves in early acute inflammatory responses from his work done in Edinburgh. His belief is that it is a CVD risk marker rather than a risk factor.

The clinical utility of high sensitivity CRP (hsCRP) was discussed in the light of the AHA/CDC statements. The usefulness of hsCRP in stroke and particularly acute stroke needs more research, but, along with blood pressure, may be of use in assessing risk.

The last speaker was Niamh Cavanagh who gave a brief talk on a study carried out in Portiuncula on hsCRP in a selected group of diabetics. When a group of normal subjects were compared to male and female diabetics it was found that the diabetic median hsCRP levels were comparable to the normal group (which had a median level higher than other studies have shown- and almost 46% were > 3 mg/L). There was a difference between male and female hsCRP levels which could reflect the difference in the treatment regimes for male and female diabetics.

All in all it was an excellent meeting, matched by the excellent lunch, the drink(s) afterwards, and -for me- the leisurely train journey home. Well done Niamh and happy retirement day.

Clinical Research Latest

Klotho

Hiroshi Kurosu et al. Suppression of Aging in Mice by the Hormone Klotho. Science 16 Sept 2005; 309: 1829-1833.

The quest for eternal life goes on! Seekers of life immemorial have seized hopefully on this research. Klotho (named after one of the three mythical Greek fates which control longevity) is a hormone that blocks the insulin/insulin-like growth factor 1 pathway ultimately leading to insulin resistance. Resistance to insulin has been shown to be an evolutionary conserved mechanism for extending life span in numerous species. Mice with a mutated Klotho gene producing excess hormone lived up to 31% longer than normal mice and had consistently higher levels of circulating insulin than normal. The opposite occurred in Klotho deficient mice. They appeared normal for about 4 weeks and then developed signs of aging such as osteoporosis and arteriosclerosis. These mice died at about 2 months, considerably shorter than the normal 24-month lifespan of the species. A couple of drawbacks however: chronic insulin resistance will eventually lead to Type 2 diabetes and fecundity is adversely affected in mice with excess circulating Klotho. Still some way to go for the Holy Grail.

New SAS Handbook

A new [booklet](#) has been produced by the Supra-regional assay service in the UK entitled **SAS Centres for Cardiovascular Biomarker Handbook**. It is intended for laboratory staff and clinicians involved in the investigation of dyslipidaemias and in the assessment of cardiovascular risk. The handbook lists available tests and the laboratories which provide them, brief descriptions of the tests, the circumstances in which they are indicated and interpretation of results.

Barry Marshall and Robin Warren win Nobel Prize for Physiology or Medicine 2005



....."for their discovery of the bacterium *Helicobacter pylori* and its role in gastritis and peptic ulcer disease"

The Lasker Prize was awarded to Barry Marshall in 1995. Quite a few Lasker awardees have gone on to win the top prize and Marshall had to wait 10 years to do so. Robin Warren was not recognised by the Lasker Foundation but it would have wrong had he not been joint winner of the Nobel Prize. He had done some of the groundbreaking work on *Helicobacter pylori* (known as *Campylobacter pylori* back then) and was the first to recognise its possible significance in the pathogenesis of ulcer formation. Their findings were at first ridiculed by the scientific community who refused to accept that bacteria could survive in an acid environment. They did not, however, reckon on the cleverness of *Helicobacter* and the tenacity of Marshall and Warren.

Notable Anniversaries

The ACBI Annual Conference takes place on the 14th and 15th of October this year. October 15th 2000 is the anniversary of the death of Konrad Bloch.

Konrad Bloch
Died 15th October 2000



Konrad Bloch was awarded the Nobel Prize in Physiology or Medicine (jointly with Feodor Lynen) in 1964 "for their discoveries concerning the mechanism and regulation of cholesterol and fatty acid metabolism". A German-born biochemist he received his initial training at the Technische Hochschule in Munich in the early 30's. Political circumstances, however, forced him to leave and he eventually took up residence in America. He became Professor of Biochemistry at Harvard in 1954 where his main area of research was on lipid metabolism, particularly unsaturated fatty acids. In 1942 Bloch and his colleagues discovered that carbon atoms of carbon - labelled acetate are incorporated into the cholesterol of the liver. In fact all of the carbon atoms of cholesterol derive from acetate. Subsequently, in a ground-breaking series of investigations Bloch was able to identify important landmarks in the series of more than thirty reactions by which the complex structure of cholesterol is built up from simple precursors. Bloch's work has contributed enormously to the study of the pathogenesis of atherosclerosis. His elucidation of the enzyme mechanisms of cholesterol synthesis has ultimately led to the discovery of statins, drugs which inhibit the first enzyme of the cholesterol pathway, HMG-CoA reductase, resulting in a lowering of blood cholesterol.

Members' Recent Publications

O'Broin S, Kelleher B, *Balfé A*, McMahon C. Evaluation of serum transferrin receptor assay in a centralized iron screening service. [Clin Lab Haematol](#). 2005 Jun;27(3):190-4.

Duffy MJ, Bonfrer JM, Kulpa J, Rustin GJ, Soletormos G, Torre GC, Tuxen MK, Zwirner M. CA125 in ovarian cancer: European Group on Tumor Markers guidelines for clinical use. [Int J Gynecol Cancer](#). 2005 Sep-Oct;15(5):679-91.

Holland J, Carey M, Hughes N, Sweeney K, Byrne PJ, *Healy M*, Ravi N, Reynolds JV. Intraoperative splanchnic hypoperfusion, increased intestinal permeability, down-regulation of monocyte class II major histocompatibility complex expression, exaggerated acute phase response, and sepsis. [Am J Surg](#). 2005 Sep;190(3):393-400.

Interesting Websites



<http://eol.jsc.nasa.gov/Coll/>

The Gateway to Astronaut Photography

Interesting collection of astronaut taken photos of Earth under various searches including cities, landscape, Earth-human interactions, hurricanes, weather etc.

<http://whyfiles.org/>

The Why Files – Science Behind the News

This website gives us a scientific explanation behind news headlines. Not surprisingly the current site is dominated by hurricanes with some informative info and photos.

<http://www.2facts.com/TSOF/science-home-feature.asp>

Facts.com – Today's Science

Extensive searchable database of science topics. Very good Hurricane Katrina coverage on current site.

World and European Clinical Biochemistry File

EJIFCC, the Journal of the International Federation of Clinical Chemistry and Laboratory Medicine has 17 articles on laboratory aspects of diagnosis, monitoring and management of tumour diseases. Topics include screening, rational use, genomics, and papers on individual markers. It can be found at

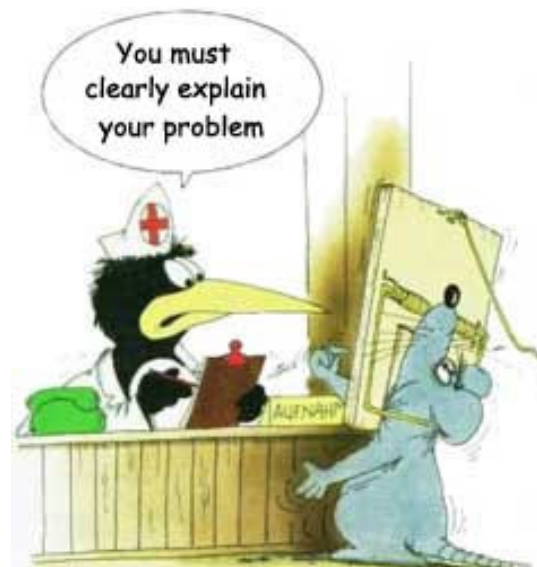
<http://www.ifcc.org/ifcc.asp>

The European Communities Confederation of Clinical Chemistry and Laboratory Medicine (EC4) has published its Strategic Plan for 2005-2008. It can be found at <http://www.e-c4.org/>

Members' News

Recently, as part of a job evaluation exercise, a number of biochemists were upgraded to either Senior or Principal Grade positions. The process is not yet completed with a number of recommended regradings still to come.

Congratulations to Orla Maguire and Margaret Sinnott on passing the final part of the MRCPATH and good luck to those who sat Part 1 in September.



Sore Throat?

Journal Watch



6

Journal of Clinical Investigation

Sudden cardiac death (SCD) can occur across a wide range of ages. It has been in the news lately in this country particularly in relation to young sportspeople. In the US 300,000 – 400,000 lives are claimed by SCD per year. The reasons for SCD are complex. The September edition of JCI has a comprehensive review outlining the interactions between functional, structural, and genetic factors underlying the risks for SCD. Possible pathophysiological mechanisms, therapeutic measures to prevent SCD, and possible ways of identifying those at risk are discussed. (M Rubart, and DP Zipes. [Mechanisms of sudden cardiac death](#) J Clin Invest 2005; 115(9): 2305-2315).

American Journal of Clinical Nutrition

Professor Mike Gibney, Professor of Clinical Nutrition Trinity College Dublin and colleagues have a review on the topic of metabolomics in the September edition of this journal. The concept of metabolomics is new to me but this article explains all. Metabolomics is defined as the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind" - specifically, the study of their small-molecule metabolite profiles. It is part of the -omics family that includes genomics, proteomics and transcriptomics which endeavours to profile specific activities of a particular cell at any given time. This may make it possible to assess the metabolic component of nutritional phenotypes and allow individualised dietary recommendations. The relationships between diet and metabolomic profiles and between those profiles and health and disease are also being investigated. (MJ Gibney et al. [Metabolomics in human nutrition: opportunities and challenges](#) Am J Clin Nutr 2005; 82: 497-503).

Case Study

Dr. Peadar McGing, Principal Biochemist, Mater Hospital, Dublin

A 21-year-old female re-presented to the hospital on Friday afternoon, 3 days after attending for a routine dermatology out-patient appointment. She had a background history of microcytic anaemia and Behcet's disease. She complained of painful mouth (5 days) and ears (4 days), burning substernal epigastric pain (2 days), and vomiting (1 day). Her medications included p.o. Prednisilone (for 6 months).

On examination she had epigastric tenderness, was pale and had mouth ulceration, including on the tip of her tongue. She complained of being unable to swallow and felt unable to tolerate p.o. intake. Accordingly IV fluid administration was initiated.

Blood tests on admission included:

Na=138, K=3.9, Urea=6.6, Creat=74; Alb=33, CaCor=2.40, PO4=0.93;

Glob=45, rest of LFT=N; wcc=12.62, Hb=9.0, MCV=66.5.

At mid-day on Saturday, on being admitted, she had repeat blood tests which showed a similar picture, including:

Na=135, K=4.0, urea=5.1; PO4=1.06, CaCor=2.23, Alb=27.

Blood tests were next performed on the following Wednesday which showed low PO4 (0.53), K (2.6) and urea (1.5). Other biochemistry parameters were essentially unchanged (incl Na=141, CaCor=2.36, creat=64).

Q. Explain the low plasma PO4, K, and urea.

Biochemistry Reference Ranges for non-pregnant Adults.

Test	Fluid	Lower	Upper	Units
Albumin	Plasma	35	53	g/L
Calcium	Plasma	2.24	2.62	mmol/L
Calcium (corrected)	Plasma	2.24	2.62	mmol/L
Creatinine (female)	Plasma	40	95	µmol/L
Globulin	Plasma	18	36	g/L
Phosphate	Plasma	0.7	1.6	mmol/L
Potassium	Plasma	3.6	5.0	mmol/L
Sodium	Plasma	133	145	mmol/L
Urea	Plasma	2.5	7.0	mmol/L

Haematology Reference Ranges for non-pregnant Adults.

Test	Fluid	Lower	Upper	Units
Haemoglobin (female)	Blood	11.5	16.5	g/dL
MCV	Blood	80.0	95.0	fL
WCC	Blood	4.00	11.00	10 ⁹ /L

Case Discussion

The patient had a 'normal' phosphate and potassium on presentation to the hospital. Both parameters changed in tandem post-admission.

Acute changes resulting in hypophosphataemia, such as in this case, are usually due to increased cell uptake of PO4. Two of the most common causes of hypophosphataemia in hospital populations are respiratory alkalosis (often caused by anxiety-induced hyperventilation) and infusion of glucose. In this patient's case her IV fluids comprised 2L N Saline (1L with 20mmol KCL) and 1L 5% dextrose over 24hrs for the first 48 hours of treatment.

A similar scenario applies in the case of potassium where acute changes are most commonly the result of altered movement of K across cell membranes.

While her potassium stores may have been reduced by extra-renal loss (vomiting) or renal loss, the primary factor in her plasma K dropping was most likely insulin effect post glucose (dextrose) load. This more than offset any benefit from KCl administered in the IV fluids.

Prior to discharge (22 days post admission) her PO4 was back to normal (1.32) but plasma K remained slightly low (3.4 at discharge, and 3.5 two months later in out-patients).

In respect to her urea it remained less than 2.0 post rehydration, indicating that her 'low' urea at the time of the low potassium and phosphate was probably her 'normal' urea level. The 'normal' urea on presentation (6.6) was in fact elevated for her, probably due to a degree of dehydration, which was corrected by the IV fluids.



Niamh Cavanagh and Helen Grimes at the West of Ireland Scientific Meeting held in Niamh's honour

Niamh Cavanagh, Principal Biochemist in Portiuncala Hospital, Ballinasloe, Co. Galway recently retired from her position. Niamh has had a long and varied career in clinical biochemistry. She started her career in Sir Patrick Dun's Hospital Dublin in 1968 and spent three years there before moving to Ballinasloe whose lab in those days was a Nissan hut with liberal numbers of rodents for company. The lab subsequently moved to a mobile home where it was so hot in summer that it was impossible to keep water baths at 37°C. They eventually moved to a new lab in 1986. When she started in Ballinasloe the staff consisted of herself, two Medical Laboratory Technicians and a full time student. Workload then was 19,000 tests per annum. Staff complement now is the Principal Biochemist and four Medical Scientists and workload has risen to 400,000 tests per annum.

Niamh is known to biochemists throughout the country through her activities in the ACBI. She has held various posts culminating in Chairman of the Association. She has seen the Association through some interesting times and was one of the people instrumental in establishing tutorials for those studying for the MRCPPath.

The above photo of Helen Grimes (on the right) presenting Niamh with a bouquet of roses was taken at a one-day scientific seminar held in Niamh's honour (see pages 2 and 3 for review). We wish Niamh a long and happy retirement.