ACB News

The Association for Clinical Biochemistry & Laboratory Medicine | Issue 670 | April 2021

In this issue

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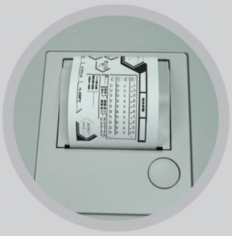

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ACB News

The bi-monthly magazine for clinical science

Issue 670 • April 2021

The Association for
Clinical Biochemistry &
Laboratory Medicine

Better Science, Better Testing, Better Care

Front cover: Simon Olpin in his jungle!

President's Message – April 2021

Welcome to the April edition of *ACB News.*

I am delighted to launch UKMedLab21 – an amalgamation of our national meetings formerly known as Focus and FiLM which this year will take place online.

Whilst we won't all be able to meet in person this time, the online nature of the event does give us the flexibility to run the programme over a longer period of time thereby offering more content to delegates. We do hope you will be able to join us and you can find out more, including how to book, on page 6.

Other items of interest in this issue include:

- An update on the progress of our COVID-19 Scientific Scholarship projects from Gemma Reidy, Adrian Shields and Joe Frost on pages 12-13.
- An article on the Trainees Discord Server which Dr Jessica Johnson, a Chem Path ST1 in Sheffield, set up as a way to connect with other Medics and Scientists in Clinical Biochemistry. This has been a great support to Trainees during the pandemic.
- An Immunology article on the UK Launch of a SCID Newborn Screening Pilot, the first DNA based screening assay in the UK.
- **The Don't Wait; Act campaign.** Doris-Ann Williams, CEO of BIVDA, has written about this campaign,

which is aimed at encouraging the general public to take more personal responsibility for their health and raise awareness of diagnostic tests.

- On pages 27-28 Hazel Borthwick explains recent proposals to expand the Pathology workforce and the ACB response.

And finally, I hope you will join me in remembering a number of ACB Members who have passed away this year including ACB Founder Members Professor Louis Woolf and Dr Ronald Robinson, and ACB Retired Members Dr Tony Kirwan and Dr Stanley J Evans.

As always, thank you for your continuing professionalism, dedication and hard work. ■

Message from the CEO

A warm welcome to ACB Members from all the staff team at Tooley Street. Well – not literally at Tooley Street . . . apart from myself, all the staff team continues to work remotely.

Plans are progressing to upgrade our virtual meeting capabilities as we anticipate a continued demand for virtual meetings based upon the success of those we organised so far and the feedback from the recent membership survey.

Thanks to everyone who completed this year's survey. This provides us with really valuable insight and information on what our members want to get from their membership. We'll be analysing carefully over the next few weeks and will report back to you in June on the emerging priorities and how we plan to action them.

We are hard at work on our annual report and review of the year's activities as well as our annual external audit and we are looking forward to welcoming members to our Annual General Meeting in June as part of **UKMedLab21**.

We've shelved any plans for face-to-face events in London until September 2021 as regulations around travel and movement remain uncertain but I am hopeful that local activity will start to pick up during the summer.

I hope you all like the fantastic cover photo of Simon Olpin's amazing jungle garden. Simon is a Consultant Clinical Scientist at Sheffield Children's Hospital and his garden has become somewhat of a celebrity having recently featured on BBC News. Read more on pages 16-17.

Thanks for your continued support of the ACB.

ACB National Meeting goes live

UKMedLab21
Online • 14-18 June

The ACB is delighted to welcome you to register for its first online national congress – UKMedLab21. The programme, which integrates the meetings formerly known as Focus and Frontiers in Laboratory Medicine (FiLM), will offer delegates the opportunity to hear from leaders in clinical science, laboratory management and education about development in policy, practice and management.

Packed with multiple sessions in two key streams – Leadership & Management and Science & Education – UKMedLab21 will help laboratory professionals at all levels to regain ground on essential CPD activity that may have been lost in 2020 during the pandemic.

We'll also be featuring a Training Day on 14th June, virtual poster sessions and awards, and an industry Expo in partnership with the British In Vitro Diagnostics Association (BIVDA).

Workshops will include moderated Q&A opportunities with speakers and presenters.

The programme overview is below and **further information and booking details can be found here.**

Registration is also offered by individual session to allow you to build a programme tailored to your interests, availability and budget.

Delegates booking a place at UKMedLab21 will receive a £50 discount on UKMedLab22 to take place on 13th-15th July 2022 at the International Convention Centre in Belfast.

Reserve your place now.

<table>
<tr><th></th><th>Monday 14th June</th><th>Tuesday 15th June</th><th>Wednesday 16th June</th><th>Thursday 17th June</th><th>Friday 18th June</th></tr>
<tr><td>09:30 – 12:30</td><td rowspan="3">ACB Training Day</td><td>President Welcome
Leadership & Management Session 1</td><td>Leadership & Management Session 2</td><td>Leadership & Management Session 3</td><td>Science & Education Session 4</td></tr>
<tr><td>12:30 – 14:00</td><td colspan="4">Lunchbreak
Industry Symposia</td></tr>
<tr><td>14:00 – 17:00</td><td>Science & Education Session 1</td><td>Science & Education Session 2</td><td>Science & Education Session 3</td><td>Medal Awards & Closing Plenary (14:00 – 15:00)
Annual General Meeting (Members Only)</td></tr>
<tr><td>19:00 – 20:30</td><td></td><td></td><td></td><td>Social Quiz</td><td></td></tr>
</table>

- ACB Training Day
- Leadership & Management
- Science & Education
- Annual General Meeting (AGM)
- Open Access and Social

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National minimum retesting intervals in Pathology

The latest version of the G147: National Minimum Retesting Intervals (authored by ACB Members Tim Lang and Bernie Croal) has now been published. This can be viewed in the ACB Resource Library: **https://www.acb.org.uk/resource/g147-national-minimum-retesting-intervals-in-pathology.html** ■

Condolences

It is with regret that we must inform you of the sad news that the following Members have passed away:

ACB Founder Member Professor Louis Woolf passed away in February, aged 101. His obituary can be found on pages 30-31 of this issue of *ACB News.*

ACB Founder Member Dr Ronald Robinson BA BSc PhD CChem FRSC, passed away aged 95. Dr Robinson was a Top Grade Biochemist at Warwick Hospital where he did much of the early work on the measurement of urinary vanillylmandelic acid (VMA).

ACB Retired Member Dr Tony Kirwan, last based in Leeds and previously of Hull Royal Infirmary, passed away on 1st March 2021.

ACB Retired Member Dr Stanley J Evans, last based in Brixworth, Northamptonshire passed away on 30th December 2020. Stan was Secretary of the FCS from 1988-1997. ■

Sudoku

This month's puzzle

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

Solution for February

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

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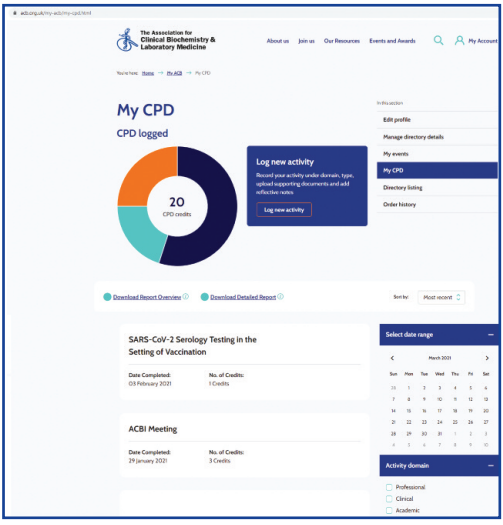
ACB digital CPD repository

Mike Lester, ACB Membership Manager

Most of our Members are under obligations with their employer and the authorities for the various registrations they hold to acquire and maintain their Continuing Professional Development (CPD), whether this be for maintaining **HCPC** or **GMC** registration, Fellowship of the Royal College of Pathologists (**FRCPath**), Chartered Scientists (**CSci**) status and many more.

As a service many members wished to see within their membership package, we are delighted to confirm that the ability to record your CPD activities, with its accompanying evidence and your reflective notes, has been delivered as part of the launch of the new digital platform in October 2020.



If you have not already done so, to access your repository first visit My Account (from the top right of your device once you **log in** to the ACB digital platform) then navigate to My CPD where you will be greeted with your CPD dashboard.

Tooltips are provided to help understand what each field means and how these can be used to get the most from this new feature. We hope you enjoy!

We want your views

There is great flexibility in how the entire digital platform has been created, including the CPD Repository. As times change so can the digital platform for members.

Are you using the CPD Repository? Is there anything in the system you would like to be able to do but are not currently able to? Or, if you have any comments at all, let me know at **mike@acb.org.uk** or +(0)20 4542 6044 and I will be very happy to discuss and learn how we can improve and deliver what you want from your membership with the ACB. ■

Congratulations

Firstly, to ACB Member Garry John who has been appointed Secretary of the IFCC Scientific Division Executive Committee, with his first three year term commencing from March 2021. We congratulate Garry on his appointment to this important role within the International Federation of Clinical Chemistry and Laboratory Medicine.

Congratulations also go to ACB Member Dr Tejas Kalaria who has been appointed Full Member-Young Scientist of the EFLM Working Group "Postanalytical Phase" (WG-POST). ■

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ACB COVID-19 Scientific Scholarships Progress Reports

supported by Abbott

In August 2020 the following members were awarded scholarship funding from the ACB (with support from Abbott) and six months on we are delighted to be able to report on their progress

Gemma Reidy

Profiling cytokine storm and markers of endothelial dysfunction during severe COVID-19 infection

The team working on the project at UHCW have scrutinised a vast amount of patient data from the CWPS CVD panel obtained between April and June, to standardise patterns of coagulation characteristics, identify patients with raised coagulation biomarkers and to define outcome groups. From this, appropriate COVID-19 positive patients with deranged coagulation, COVID-19 positive patients with no disturbance in coagulation and healthy controls have been identified so far. Further cases scrutiny was carried out to harmonise across group variables around age, sex and comorbidities. For these patients a number of samples have been retrieved from Arden Bio-bank storage.

We started measuring a panel of cytokines and endothelial markers of dysfunction; during this initial phase of the project we have established that samples exhibit adequate stability and the levels of biomarkers of interest are indeed within the measurable range.

In parallel we started measuring autoantibodies associated with anti-phospholipid syndrome and vasculitis.

A small set of samples from COVID-19 positive patients with deranged coagulation have also been analysed for initial characterisation, which has confirmed that Neutrophil to Lymphocyte ratio (NLR) and IL-6 levels correlate with death and mortality rates.

This information will be considered when evaluating the significance of cytokines, endothelial markers of dysfunction and autoantibodies on patient outcomes.

Adrian Shields

Can the measurement of anti-SARS-CoV-2 salivary antibodies enhance the sensitivity of seroprevalence studies and are these antibody responses clinically relevant?

In 2020, the ACB generously funded our ongoing investigations

into the utility of saliva as a diagnostic fluid for SARS-CoV-2 antibodies. In collaboration with University Hospitals Birmingham NHS Foundation Trust and Birmingham Community Hospitals NHS Foundation Trust the COVID-19 Convalescent (COCO) immunity study has collected over 3,500 paired serum and saliva samples from healthcare workers following natural infection and immunisation with the Pfizer BioNTech vaccine to pursue this work.

We previously developed an assay designed to detect the total antibody response (IgG, IgA and IgM) directed against the SARS-CoV-2 spike glycoprotein following mild COVID-19 infection for the purposes of seroepidemiological studies. Repurposing this assay to measure salivary antibodies has proved challenging, particularly with respect to achieving a desired diagnostic specificity of greater than 90%. Instead, assays that measure each immunoglobulin isotype in isolation have been developed. Using these assays, we have confirmed that anti-spike IgG and IgM responses are easily detected in saliva of approximately a third of individuals who have serum antibodies. However, the IgA isotype produces far greater non-specific background activity in both our individual and combined assays that requires further development.

Preliminary data from one of our healthcare worker cohorts suggests that unstimulated, expectorated saliva is unlikely to be a satisfactory replacement for blood sampling for the purposes of performing seroprevalence studies (manuscript in preparation).

Further work is ongoing to investigate whether stimulated salivary collection, which enriches for gingival crevicular fluid, will prove more promising for this purpose. Our preliminary data regarding vaccine responses to the Pfizer BioNTech vaccine is available as a pre-print (Shields AM *et al.* Longitudinal protection following natural SARS-CoV-2 infection and early vaccine responses: insights from a cohort of community based dental healthcare professionals. MedRxiv – doi.org/10.1101/2021.02.24.21252368) and we look forward to updating the ACB and its members about the work characterising the salivary responses in this cohort later.

Joe Frost

Linking iron with inflammatory profiles and clinical outcomes in COVID-19

Thanks to generous ACB funding we have measured serum iron in two cohorts of COVID-19 patients from the first wave, confirming our previous results that serum iron associates inversely with disease severity. We are now measuring proteins in serum that control iron homeostasis (hepcidin and erythroferrone). To complement these investigations, we have also been assessing how different proteins that mediate harmful inflammatory responses correlate with perturbed iron status in COVID-19.

ACB reacts to BBC Panorama – 'Undercover - Inside the Covid Testing Lab'

Neil Anderson, ACB President

Statement on BBC Panorama – 'Undercover - Inside the Covid Testing Lab' broadcast on Monday 29th March 2021, 7.30pm BBC1

The ACB is a world leading professional membership organisation dedicated to the practice and promotion of the highest standards in laboratory testing and patient care.

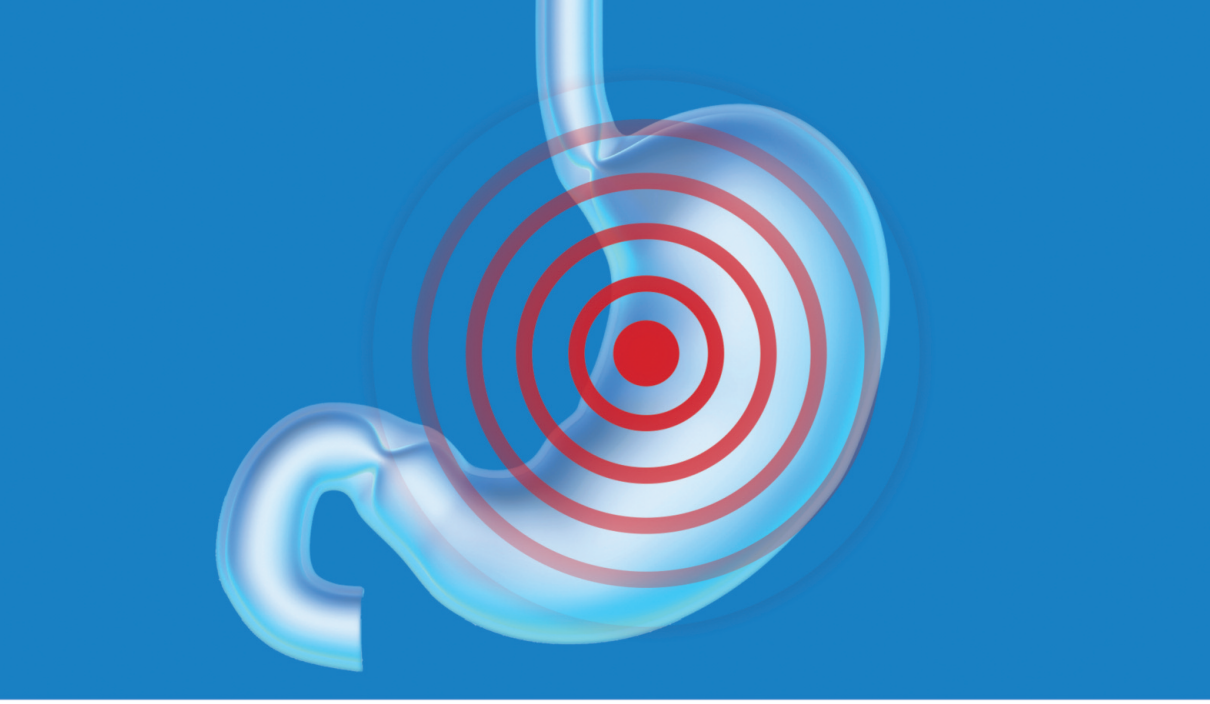
The practices exposed by BBC Panorama 'Undercover – Inside the Covid Testing Lab' on Monday 29th March point to a lack of leadership and professional rigour which falls well below the standards that patients and the young hardworking scientists in this laboratory should expect.

The majority of ACB Members work in the NHS which relies on a workforce of qualified, registered and regulated scientists who take the utmost care when processing patient samples. Healthcare Scientists take pride in their work and ensure that the highest quality and safety standards are met when processing patient specimens for COVID-19 and other conditions. Molecular tests such as PCR require strict adherence to protocols, specialist training and ongoing quality assurance (including environmental monitoring) to reduce the risk of contamination. UK diagnostic laboratories are accredited and inspected to ensure that high quality standards are met and maintained. Ensuring that the correct result is obtained in a timely manner is the paramount concern of those working in diagnostic laboratories. Every specimen represents a patient, and every patient matters.

NHS Pathology laboratories are subject to rigorous accreditation, professional standards and ongoing quality assurance, in order to give confidence to patients regarding the standard of care in our laboratories. In this case we would particularly welcome the views of the Health and Care Professions Council (HCPC) and the UK Accreditation Service (UKAS) regarding the practices exposed in the programme.

For further information please contact: **enquiries@acb.org.uk**

- **Click here** to view the full programme on BBC iPlayer. ■



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30 years to grow a jungle

Dr Simon Olpin

As a small boy I had a fascination with living creatures, especially amphibia and reptiles. Indeed, my fascination with snakes resulted in spending five days in hospital following an adder bite at the age of sixteen.

As time went on my love of the natural world encompassed plants and particularly exotic plants. However, the prospect of travel to tropical jungles was prematurely ended after a terrifying flight to the South of France where I vowed never to repeat the experience.

My wife Julie and I moved to Sheffield from Cambridge in 1987 as I was fortunate in getting a job as a Clinical Biochemist working with Dr Rodney Pollitt on Metabolic Disease in the MRC Unit at Middlewood Hospital. We moved the following Spring to Sheffield Children's Hospital.

We bought a house with quite a large garden of approximately 40 x 250 feet and I set about transforming a fairly blank canvas of predominantly lawn and a few flower borders into something a bit more exotic. I had a fascination with jungles fuelled particularly by the David Attenborough BBC wildlife programmes I had grown up with.

On a family holiday in 1991 we visited The Lost Gardens of Heligan and that experience coupled with the BBC series *The Lost Gardens of Heligan* was a tremendous inspiration for my desire to create my own little version of a jungle in Sheffield. It wasn't easy as many "exotic" plants were lost through trial and error. I grew many cannas, bananas, gingers and tender palms during the summers but these had to be brought into our conservatory in winter. It was when I started to concentrate more on cordylines, phormiums, bamboos, tree ferns, eucalypts, acacias, umbrella trees (Sheffleras), European Fan palms and particularly the Chinese Windmill Palm that a more permanent "jungle" began to emerge. In addition to these plants I acquired a range of rare and unusual plants which added to the diverse range of plant structure, leaf size, shape and form. Many of these plants originated from high altitude provenances from around the world although the overall theme is one of South East Asia.

I lost quite a lot of plants in the very cold winters of 2010 and 2011 but surprisingly many plants came through, although some not without damage. However, increasingly my interests have encompassed the breeding of poison dart

frogs which fits nicely with the jungle theme!

Now after over thirty years we have a mature jungle garden which you walk through and under. There are many bamboo species, some with culms up to 30 feet, over 40 large palms, many with trunks of 12 to 20 feet, some lovely umbrella trees, several large tree ferns and two notable eucalypts grown from seed which are now over 80 feet in height!

It may be Sheffield but it's our own little slice of "jungle". ■

- Simon's jungle recently featured in the press with the **BBC** and **The Telegraph,** covering his story!

Future AQMLM Zoom Meetings

AQMLM

Jonathan Middle, Chair, AQMLM

We are confirming our next three Zoom Meetings, as follows:

- **Zoom 11** – 11:00 Wednesday 7th April 2021
  Diagnostic Sensitivity & Specificity, Prevalence and Predictive Value
- **Zoom 12** – 11:00 Monday 10th May 2021
  Quality Challenges in Genomics, Cellular Pathology and Blood Products Delivery
- **Zoom 13** – 11:00 Tuesday, 22nd June 2021
  Pre-Analytical Quality Challenges

Registration is open for Zoom 11 – details are available here: **https://www.aqmlm.org.uk** . (Currently, 35 places have been allocated.)

Full AQMLM members with annual subscriptions may also pre-register for Zoom 12 and Zoom 13. Please do not leave it too late to register! ■

LAB TESTS ONLINE UK

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Produced by The Association for Clinical Biochemistry & Laboratory Medicine

With support from The Royal College of Pathologists — Pathology: the science behind the cure; IBMS

Lab Tests Online-UK is a non-commercial website written by practising laboratory medics and scientists with lay editorial review of content to ensure its suitability. The aim of the website is to help patients and the public, including healthcare professionals, understand the many clinical laboratory tests that are used in diagnosis, monitoring and treatment of disease.

What's New on Lab Tests Online-UK?

On the back of COVID-19 work, NHS Wales launch a new register for patients with rare diseases. See the website for more information.

LTO-UK fact of the month

If you printed off all the pages of LTOL-UK and laid them end-to-end, they would stretch a long way, but probably not as far as the distance the Treasurer cycled across the USA.

Meet the Committee

This month it's the turn of our Treasurer, Mike Bosomworth.

After retiring as Clinical Lead for Blood Sciences and Specialist Laboratory Medicine from Leeds Teaching Hospitals Trust in September 2016, he was persuaded to become Finance Director for the ACB and, to his surprise, automatically became the LTO-UK Treasurer.

Otherwise, he is a Parish Councillor and Chair of his village Sports Club. He supports a local charity called Open Country, which takes disabled people into the countryside.

He has completed a number of challenges to raise money for brain research e.g. cycling unsupported east/west and west/east across North America and climbing Kilimanjaro. He's unsure what his next major fund-raising challenge will be, but as always it will be entirely self-funded. He celebrates his 45th wedding anniversary later this year. Mike has two daughters, one son, two granddaughters (aged 4 and 2 years) and one grandson (age 3 months).

He is trying to finish renovating the family home (25 years into a 5 year project), cycles regularly both on- and off-road; takes on the occasional triathlon; and would like to attempt an Ironman sometime soon. He also occasionally goes fly fishing.

Despite being, in his own words, of (very) late middle-age, he is busier than ever. Oh, and he also owns a classic car, a Triumph Stag!

Get involved

Join the editorial team

If you are interested in contributing to the vital work of the editorial team to keep the website up-to-date and to introduce new material please contact us for more information.

Become a Lab Tests Online-UK champion

Join our champions and promote LTO-UK locally and nationally. Champion packs provide a great starting point with ideas and marketing materials, for more information or to join our champions contact us.

Email: **labtestsonlineuk@acb.org.uk** Website: **labtestsonline.org.uk** Follow us

Association of Clinical Pathologists

Chemical Pathology virtual monthly Zoom webinars 2021

Thursday 15th April 13:00-14:00
Lipids: Investigation & management of hypertriglyceridaemia – *Dr A Wierzbicki*

Thursday 13th May – *To be confirmed*

Thursday 10th June 13:00-14:00
C-peptide in blood and urine clinical value – *Dr T MacDonald*

Thursday 8th July – *To be confirmed*

August Summer Break

Thursday 9th September 13:00-14:00
Lipids: PCKS9 inhibitors and novel lipid lowering agents – *Dr D Preiss*

Thursday 14th October 13:00-14:00
Nutrition: Nutritional concerns before and after bariatric surgery – *Dr C Le Roux*

Thursday 11th November 13:00-14:00
Parenteral nutrition – *Dr W Simpson*

Thursday 9th December – *To be confirmed*

If you would like to register for the meeting,
please email Rachel Eustace at rachel@pathologists.org.uk
ACP members: free of charge (conditions apply)
Non-Members: £10 per webinar or £50 for the year

Publication Deadlines

To guarantee publication, please submit your article by the 1st of the preceding month (i.e. 1st May for June 2021 issue) to:

editor.acbnews@acb.org.uk

We try to be as flexible as possible and will accept articles up to the 20th to be published if space allows. Otherwise they will be held over to the next issue.

If we are aware that articles are imminent, this gives us more flexibility and we can reserve space in anticipation.

If in doubt, please contact Gina Frederick, Lead Editor, via the above e-mail. ■

FCS briefing: pay update

Mike Cornes, FCS Staff Council Representative

Pay update – 21st March briefing

You will have seen in the news recently that the government have put forward their recommendation in their evidence to the NHS Pay Review Body (PRB) that a pay rise for NHS staff should be limited to 1% (**https://www.gov.uk/government/publications/dhsc-evidence-for-the-nhsprb-pay-round-2021-to-2022**).

We would like to update you on what the FCS is doing via its involvement with the wider NHS Trade Union leads. Collectively, we have enlisted a media professional to support us in putting together our own evidence to the PRB (which has now been submitted) and in campaigning to support this via media and engaging with key leaders including MPs. You will have seen some of these, including NHS Providers, which represents NHS Trusts, already speaking out for better than the 1% recommendation as promised in the NHS People Plan.

Part of the media campaign involves a website which you can look at with various information and resources to support the Trade Union's case for a pay rise. The website can be found at: **www.withnhsstaff.org**

What the Trade Unions have stated all along is that we want to see an "early and significant pay rise" and assurance that the PRB body's recommendations will be adhered to and funded.

By NHS Unions and allies across the labour movement working together, we are seeking to change the conversation around the pay review process, to ensure that investing in NHS pay is recognised as a sensible and affordable economic intervention that will support the economy and population in its recovery via the 5 pillars below:

1. The austerity agenda of 2010 of public spending restraint failed and only served to stagnate growth in the economy. A different approach is required to support the UK economic recovery in 2021.
2. In the Budget on 3rd March the Government should be looking to support the economy with a positive stimulus to help it to bounce back quickly.
3. A pay increase for NHS staff is a sensible economic stimulus that will reach every community and corner of the UK.
4. The cost of a pay increase is offset significantly by the economic return to the Treasury in the form of income tax, other direct and indirect taxes, and savings on benefits and pensions contributions.
5. An analysis by "London Economics" commissioned by the unions showed that a 10% increase in the Agenda for Change pay bill would have a net cost of just £0.66 bn. ■

The Diggle Microbiology Challenge

These multiple-choice questions, set by Dr Mathew Diggle, are designed with Trainees in mind and will help with preparation for the Microbiology Part 1 FRCPath exam.

Question 23 from February's ACB News

Can you link the most likely antiviral agents with the indication?

A. Ganciclovir
B. Aciclovir
C. Simeprevir
D. Amantidine
E. Oseltamivir
F. Foscarnet
G. Peginterferon alfa-2a

1. Generally healthy adult with chronic HBV infection
2. Person with chronic HCV infection
3. Person with ganciclovir-resistant CMV infection
4. Elderly lady with localised zoster presenting within 72 hours of onset of rash
5. Lady with confirmed INFB presenting within 48 hours of onset of symptoms.

Answers – 1-G, 2-C, 3-F, 4-B, 5-D.

Question 24

Which is the best specimen to send to the Microbiology laboratory for diagnosis of infection?

A. Blood
B. Urine
C. CSF
D. Vitreous humor
E. Biopsy of colon
F. Skin biopsy from nape of neck
G. Stool
H. Nasal Pharyngeal swab

1. Profoundly immunosuppressed patient with funduscopic evidence of retinal necrosis.
2. Person with history of dog bite who is confused, agitated and exhibits hydrophobia.
3. Recent elderly inpatient with perfuse diarrhoea.
4. Person with flu-like symptoms with recent contact with COVID-19 positive person.
5. Person post bone marrow transplant, bloody diarrhoea and neutropenic.

The answer to Question 24 will appear in the next issue of ACB News – enjoy!

UK to Launch SCID Newborn Screening Pilot; The first DNA based screening assay in the UK

Sarah Beck, Consultant Clinical Scientist, Immunology, University Hospitals Birmingham

What is SCID?

Severe combined immunodeficiency (SCID) is a medical emergency. Children are born with absent or non-functional T-cells, a major component of the adaptive immune system leading to profound abnormality of both the cellular and humoral immunity. It is currently estimated that 15-25 children a year are born with a form of SCID (incidence ~1 in 50,000).

Children with SCID are susceptible to recurrent and severe life-threatening infections. The life expectancy of these children, if untreated, is usually 1 to 2 years. There are phenotypic variations of SCID ranging from absent T-cells, B-cells, and NK cells, to 'leaky SCID' where minimal concentration of T cells are present but normal function is lacking. Confirmation of the cellular phenotype is performed by flow cytometry analysis, usually in Immunology laboratories. Further genetic testing is undertaken to confirm specific mutations attributed to phenotypes.

Why should SCID be included in newborn screening?

Currently diseases included in newborn screening (NBS) include sickle cell disease, cystic fibrosis, congenital hypothyroidism and inherited metabolic diseases; incidence of these diseases range from ~1 in 2000 to 1 in 150,000. Screening for rare diseases enables rapid interventions, thus improving patient outcomes.

All SCID variants may be treated with autologous haematopoietic stem cell transplant (HSCT), which repairs the damaged immune system. Some variants can be treated with gene therapy, correcting the defective gene. It has been well established over recent decades that survival for SCID patients is significantly improved by earlier treatment, largely by limiting severe infection prior to transplant. Many studies have shown that transplant occurring soon after birth increases the probability of >2 year survival to >90%. Newborn screening for SCID is not a new idea. The first pilot was in Wisconsin, USA in 2008. Since 2019 all 50 US states include screening, with 100% routine coverage in New Zealand as well as screening programmes in many European countries.

At the recent virtual meeting of the International Society for Neonatal Screening (ISNS) on 26th and 27th January 2021, speakers from across the globe shared their experiences of SCID NBS. The common take-home message was that NBS for SCID is cost effective, with earlier diagnosis resulting in optimal treatment and better outcomes for patients. All countries offer the same

screening principle of initial testing undertaken by T-cell Receptor Excision Circle (TREC) analysis followed by flow cytometric analysis of lymphocyte immunophenotypes.

What is a TREC?

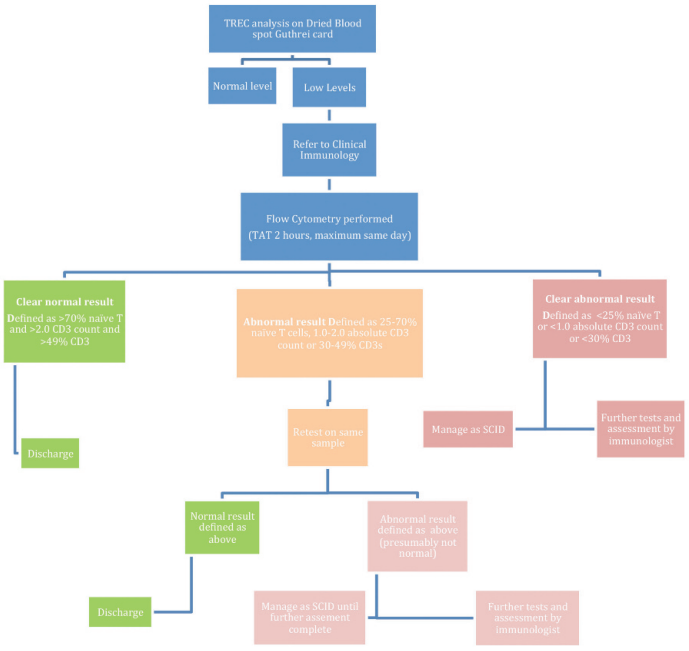
A T-cell Receptor Excision Circle (TREC) is a section of DNA that is produced during T-cell development (T-cell receptor rearrangement) in the thymus. This can be used as a marker for thymic activity. Significant T-cell abnormalities result in significantly lower numbers of TREC produced. TREC can be quantified by real time PCR, and due to the high analytical sensitivity of amplifying DNA, testing can be performed on small volumes (3 µL) of blood. A method has been well established utilising the dried blood spot Guthrie cards.TREC testing could therefore be performed as part of the newborn screening process that occurs for all babies born in the UK. Patients found to have low TREC could then be referred for lymphocyte phenotyping to confirm the absolute concentrations of T, B and NK- cells.

How will the UK Pilot scheme run?

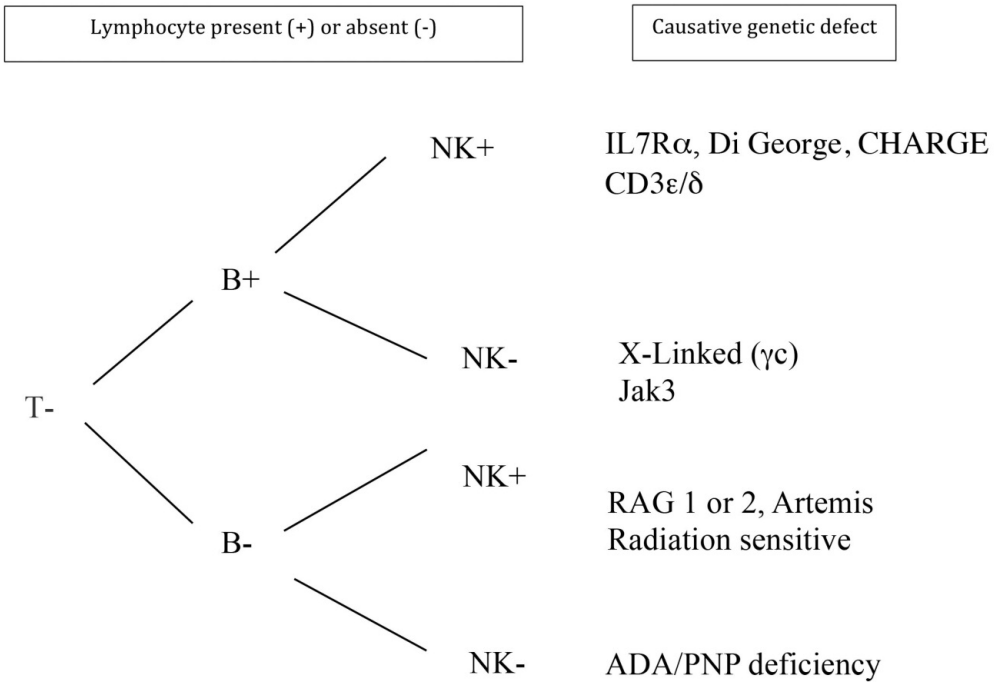
From September 2021 the UK will launch a pilot screen for SCID utilising TREC testing at six NBS centres (North London, Southeast London, Newcastle, Birmingham, Manchester and Sheffield). This will be the first time DNA testing has been used for newborn screening.

Children found to have low TREC will be referred to a Regional Immunology Centre (Great Ormond Street Hospital, Newcastle, University Hospitals Birmingham, Manchester Royal Infirmary, Northern General Hospital Sheffield, Nottingham University Hospitals or Leicester Royal Infirmary) where urgent flow cytometric analysis will be performed. This will enable rapid patient management where appropriate, or discharge on the same day (Figure 1 – Screening process flow chart).

Figure 1 – Screening process flow chart



SCID variants defined by lymphocyte phenotype



This pilot scheme will only cover 2/3 of babies born in the UK; some sites have been selected due to higher frequency of disease prevalence, most commonly attributed to consanguinity.

In the UK it has been agreed that a pilot scheme will run for 2 years to assess the effectiveness of screening for this condition. The UK National Screening Programme has posed two questions in particular for the duration of the pilot scheme:

1. How many babies may be diagnosed with SCID when they do not have the condition (false positives)?
2. What care and treatment could be offered to babies with other conditions that cause low numbers of white blood cells?

Immunologists in the UK as well as the associated primary immunodeficiency societies and patient groups welcome this pilot to see what positive benefits this will bring to patients – exciting times ahead! ■

Deacon's Challenge Revisited

No 13 - Answer

1. *A patient was mistakenly given 500 mL 20% mannitol ($C_6H_{14}O_6$) intended for the patient in the next bed, instead of the same volume of normal (0.9%) saline. Calculate the extra osmolal load given over that which would have resulted from isotonic saline.*
2. *A patient known to have diabetes insipidus is admitted in a coma. His plasma osmolality is 324 mOsm/Kg. If his weight is 85 Kg, estimate his body water deficit.*

MRCPath May 2001

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1. Osmolal load (mOsm) $= \frac{\text{Total given (mg)}}{\text{MW}}$

   Since the total amount given (mg) = Concentration of fluid (mg/L) x Volume given (L)

   Then, osmolal load (mOsm) $= \frac{\text{Concentration of fluid (mg/L) x Volume given (L)}}{\text{MW}}$

   For mannitol:

   Concentration of fluid = 20% = 20 g/100 mL = 200 g/L = 200,000 mg/L

   Volume given = 500 mL = 0.5 L

   MW ($C_6H_{14}O_6$) = (6 x 12) + (14 x 1) + (6 x 16) = 182

   Osmolal load $= \frac{200{,}000 \times 0.5}{182}$ = 550 mOsm (2 sig figs)

   For saline:

   Concentration of saline = 0.9% = 0.9 g/100mL = 9 g/L = 9000 mg/L

   N.B. this concentration must be multiplied by 2 since each molecule of NaCl (unlike mannitol) dissociates to give two osmotically active species (Na^+ + Cl^-).

   Therefore, osmotic concentration = 9000 x 2 = 18000 mg/L

   Volume given = 500 mL = 0.5 L

   MW (NaCl) = 23 + 35.5 = 58.5

   Osmolal load $= \frac{18000 \times 0.5}{58.5}$ = 150 mOsm (2 sig figs)

   Extra load = Load of mannitol - Load of saline

   = 550 - 150 = 400 mOsm

2. **Assumptions:**

Normal initial osmolality e.g. 284 mOsm/Kg

Pure water loss has occurred so that there is no change in the total osmotically active species.

Water loss is shared between all body fluid compartments.

Total initial osmotic species (mOsm) = Total final osmotic species (mOsm)

Ignoring the small difference between osmolality and osmolarity:

Total osmotic species (mOsm) = osmolality (mOsm/Kg) x Fluid volume (L)

Therefore:

Initial osmolality x Initial vol = Final osmolality x Final volume…… (i)

Initial osmolality = 284 mOsm/Kg

Final osmolality = 324 mOsm/Kg

It is unclear whether the body weight was obtained before or after the fluid loss (it is very difficult to weigh an unconscious patient and if he has been attending as an outpatient for his diabetes insipidus then a recent body weight is probably available). It actually makes little difference to the final answer and the calculation is more straightforward if 85 Kg is assumed to be his initial weight. Assuming the body was initially 60% water, then

Initial vol = Body wt (Kg) x 60/100 = 85 x 0.6 = 51 L

Substitute these values into equation (i), rearrange and solve for the final fluid vol.

284 x 51 = 324 x Final vol (L)

$$\text{Final vol (L)} = \frac{284 \times 51}{324} = 45 \text{ L (2 sig figs)}$$

Fluid deficit (L) = Initial vol (L) - Final vol (L)

= 51 - 45 = 6 L

N.B. *The term **osmolality** refers to the concentration of osmotically active species per **Kg of solvent,** whereas **osmolarity** is the concentration expressed **per litre of solution.** In clinical biochemistry we make so many approximations whenever we use osmolality/osmolarity that the small difference is rather academic.* ■

Question 14

A buffer is required for an enzymatic assay which has a pH of 7.4 and total phosphate concentration of 100 mmol/L. Calculate the amounts of anhydrous sodium dihydrogen phosphate and disodium hydrogen phosphate which need to be weighed in to make 1 L of buffer. The pK of the dissociation is 6.82 (atomic weights: Na = 23, P = 31).

MRCPath November 2001

The future of the diagnostic workforce

Hazel Borthwick, ACB Director for Education, Training and Workforce

There is no doubt that the COVID-19 pandemic has been the largest challenge facing the NHS. Whilst there is much publicity about the impact on front line patient-facing roles and wards, it is noteworthy that Pathology is considered in this context. Whilst NHS laboratories responded extremely well with existing staffing and infrastructure, it is also recognised that existing resources were not at a sufficient level to prepare for the arrival of the pandemic.

Prioritised for review within the NHS is a proposal to increase the diagnostic workforce capacity and capability. The ACB welcomes this. A Pathology Workforce Group has been developed that will identify a series of principles and actions that can be implemented across the short to long-term, to secure workforce capacity where needed, and ensure a sustained pipeline of staff with the skills required to deliver diagnostics for the future. It aims to help regional teams by boosting local diagnostic capacity and capability.

The ACB was invited to review the draft paper and has several members on this group. The general aims of the project are very much supported by the ACB. It highlights that investment and reform are required as part of the NHS long-term plan and that the demands on diagnostic laboratories will increase post-pandemic. Laboratories will be fundamental in supporting Trusts to get back to business as usual with recovery plans and tackling of long waiting lists.

The paper also discusses the introduction of Community Diagnostic Hubs (CDHs), a new service delivery model which will provide COVID-19-minimal, highly productive elective diagnostic services for cancer, cardiac, respiratory and other conditions. These CDHs will aim to address the shortfall in diagnostic capacity and will undoubtedly involve expanding the role of healthcare professionals. The group aims to provide direction for a more flexible workforce with improved learning opportunities, to recruit additional staff and for better workforce planning.

Following a review of the document, the ACB submitted feedback to the Workforce Group that required additional consideration and inclusion. This was welcomed by the group and has ensured that Clinical Scientists within Laboratory Medicine are considered key contributors to the diagnostics workforce. The qualities and training of Clinical Scientists have shown how adaptable and flexible the profession is in contributing to the many facets of Pathology delivery, especially during this pandemic. This is especially important when considering the Pathology specialities of Microbiolology/ Virology and Haematology. Clinical Scientists are, and have been, an invaluable resource for service development and test implementation throughout the pandemic and can contribute significantly to the aims outlined. STPs can be utilised in the delivery of both immediate and long-term Pathology plans. Clinical Scientists will be vital in the delivery of CDHs. The Clinical Scientist's role, acting as the liaison between medics and the laboratory,

alongside their experience of setting up services, validation and verification of methods and patient facing roles in existing hospital clinics, will be an asset going forward and this must be included and recognised.

The expansion of roles is being considered and developed by patient group directive work and is an opportunity that will be included in the work of the Pathology Workforce Group. This presents us a unique opportunity to further develop the role of Clinical Scientists, as we have seen in some areas of the country in lipid and endocrine clinics. Prescribing will play an important part of enhanced roles within Pathology and the wider healthcare system and this needs to be further developed within the plans.

All disciplines were impacted by the pandemic in different ways and it is recognised that all disciplines have current workforce challenges. We are recommending that the overall Pathology workforce strategy would benefit from a shift in tone to ensure that the aim of a multi-professional diagnostics workforce is achieved. The ACB has highlighted that there are significant shortcomings in current service provision, especially in recruiting to roles within Laboratory Medicine. Nationally we are under-recruiting for planned retirements and more financial support is essential to enable Trusts to take on Trainees. Many Trusts are reporting that they are failing to recruit because the bank of applicants does not exist. The ACB welcomes the expansion of the training programme for Pathology. Within that expansion there must be a consideration of competencies and a removal of barriers to apply. Pathology must become an inclusive environment that can respond to the challenges that lie ahead. This must include reviewing restrictions to entry into the Pathology professions, and a more modular approach to training, for example why would a post-doc with experience in Pathology research be required to go through the full STP and HSST programme?

The expansion of the HSST programmes in Histopathology is outlined, as is an increase in the number of HSST training places in Microbiology. However, an increase in the numbers of HSST positions across Pathology disciplines is required if laboratories are going to deliver the aims. The National School for Healthcare Science (NSHCS) alongside the IBMS have opened up the HSST entry requirements, which will increase numbers of those who can enter the programme to facilitate development of the workforce. This is to be welcomed. HSST posts have been challenging to fill and expanding the programme to other scientists is a welcome step forward. However, given that within some disciplines there are clear differences in roles between Clinical Scientists and Biomedical Scientists, the ACB is working with NSHCS to ensure that there is clarity of roles, recognising the differences in HCPC registration, titles and standards. There is a great deal of change currently occurring within our laboratories and profession and it has been a very challenging year. There are positives that will come from the efforts faced by laboratories throughout the pandemic. Scientists and laboratories have been at the heart of helping the nation in managing its response to COVID-19 and hopefully now the investment and resources that were lacking will start to be addressed.

If any member would like to comment or give feedback on any of the topics discussed within this article, or would like to raise any other issues that are facing your teams and feel ACB input may help, please contact the ACB at **enquiries@acb.org.uk** ■

Join the Clinical Biochemistry Trainees Discord Server

Dr Jessica Johnson, Sheffield Teaching Hospitals NHS Foundation Trust

The Clinical Biochemistry Trainee Discord server was set up in January by Dr Jessica Johnson, a Chemical Pathology ST1 in Sheffield, as a way to connect with other Clinical Biochemists, be they medics or scientists.

It was especially helpful in the pandemic where face-to-face training days and conferences have been on hold, and so getting to know people in other centres has been more of a challenge than usual, in addition to the challenges of being quite a small specialty in general. It is mostly aimed at Trainees as an informal way to ask questions about general training, exams, revision tips and other things that might come up in our day to day getting to grips with things, however, more senior members are always welcome to share their vast wealth of experience and insights.

So far over 100 people have joined, and this has allowed for Trainees to connect with each other, not only within the UK, but also as far afield as Turkey and Australia. Topics have included general enquiries about exams and revision sessions, useful websites for learning, swapping tips on coding (as well as highlighting great resources for beginners), and even time for the occasional joke or two! We have also recently set up a server bot which members can use to add flashcards for revision which anyone can then access.

The beauty of Discord is the ability for people to choose which topics they are interested in, so if you're not interested in a topic, it can be muted. It is free, and easily accessible via phone, browser, or computer app.

We are still growing and evolving, and would love to have more people join in! Also, we welcome any feedback for how the server might be improved. ■

Join the Clinical Biochemistry Trainees Discord Server!

Check out the Clinical Biochemistry Trainees community on Discord - hang out with 122 other members and enjoy free voice and text chat.

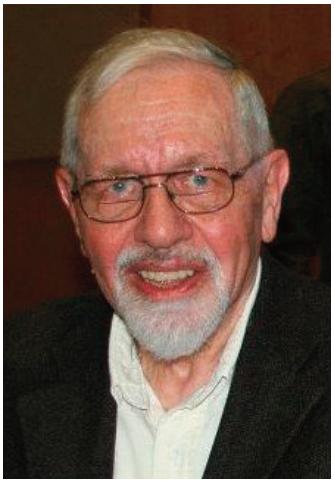
discord.gg

A Tribute to Louis Isaac Woolf

24th April 1919 – 7th February 2021

Professor Louis Woolf died aged 101 from a heart condition on Sunday 7th February 2021 in Vancouver, British Columbia. He is best known for his pioneering work conceiving and developing a dietary treatment for phenylketonuria based on a phenylalanine – depleted hydrolysate of milk protein.

Louis was a Founder Member of the Association for Clinical Biochemistry and Laboratory Medicine from its inception in 1953 and he remained a Member until his death.



He was born in London and brought up in Hackney, the third child of Jewish immigrant parents from northern Romania.
He gained scholarships to study at University College London (UCL), firstly for a degree in Chemistry achieving First Class Honours, and subsequently for a PhD.

In 1939, at the outbreak of World War II, along with the rest of UCL, he was evacuated to Aberystwyth in Wales and it is there he met his future wife, Frances Mary Richards. They married in Welshpool in 1943.

In 1944 he took a research post at pharmaceutical and special dietary products manufacturer Allen and Hanbury based in Ware, north of London. It is now owned by GlaxoSmithKline. One of their important food products was casein hydrolysate. Across the site in their Research Department Louis developed new pharmaceuticals, notably a new antacid, dihydroxyaluminiumamino-acetate, and also attempted to purify the company's proprietary penicillin.

In 1947 he secured an Imperial Chemical Industries funded post at Great Ormond Street Hospital (GOSH), to research tyrosine metabolism in premature babies. He was provided with a laboratory on the 4th floor entirely for his own use. Converting a balcony into a makeshift fume hood, he introduced and developed the exciting new technique, known only since 1944, of 2-dimensional paper chromatography for his studies of urine amino acids. His laboratory thereby became one of the very few in the UK to do so. In what was to become a significant encounter, he was visited by a German doctor, Horst Bickel, who asked to spend a number of weeks as laboratory observer. Bickel was en route from Zürich Kinderspital in Switzerland to a new post at Birmingham Children's Hospital. On one of the occasions when Bickel returned to see Louis in London, Bickel enquired whether Louis could think of a way to treat the disorder phenylketonuria (PKU). Louis indeed had a concept he had been unable to translate into practice as he could not persuade paediatricians at GOSH to trial it with their PKU patients. This involved the removal of phenylalanine and aromatic amino acids from an acid hydrolysate of protein, for example casein, by filtration through charcoal and adding in essential nutrients. Whilst allegedly sceptical of Louis' idea, Bickel in fact successfully treated a 2 year old girl with PKU in Birmingham, utilising Louis' method for producing a liquid food

low in phenylalanine content. Casein hydrolysate was obtained from Allen and Hanbury's. This was a world first with a lasting legacy.

Less well known is Louis' conviction since his time at GOSH that newborn screening would improve PKU outcomes by allowing earlier treatment. Urine testing was a simple and non-invasive way and he and Senior Medical Officer in Public Health, Dr Nancy Gibbs, trialled the first ever community based urine screening programme of the general newborn population. This was aimed at detecting all cases of PKU in a cohort of babies in Cardiff, Wales from 1958 to 1959 and was partially successful. Louis' knowledge and expertise in the field of PKU was becoming increasingly recognised. Accordingly, he was invited to join two working groups reporting to the UK's Medical Research Council on detection and treatment of PKU in 1963 and 1968. By then it was apparent that urine detection in newborns was not sufficiently reliable, and blood analysis became the recommendation with the heel prick test we are now so familiar with.

Louis' published work was noticed by Dr William Gibson from the University of British Columbia (UBC), and Louis was invited there to present a summary of his work to date at a conference on biochemistry and mental illness in 1967. He left such an impression that the following year Gibson offered him a post which he took up as Associate Professor at UBC, with promotion to Professor following 6 years later in 1974. He published extensively with over 120 papers to his name, a book on renal tubular dysfunction written in Oxford and he contributed to books, conferences and supervised many research students. The Editors of the 7th, 1970 and 8th, 1986 Editions of *Geigy Scientific Tables* acknowledged Louis' 'intensive collaboration' in connection with the chapter entitled Inborn Errors of Metabolism. He retired in 1984 after a 16 year teaching and research career at UBC.

Never losing his love of chemistry and biochemistry, Louis continued to attend scientific meetings around the world in his retirement. Possibly his last trip abroad was in 2003 when he was 84 and one of the guests of honour as a Founder Member at the Association's Golden Jubilee meeting in Manchester (pictured left).

A shy and modest man, he was devoted to his family. His wife Frances died in 1991 and Louis is survived by his only daughter Lesley, grandsons Benjamin and Oliver, two great-grandchildren, Graham and Willow and his youngest brother, Henry. He was beautifully spoken in an old-fashioned English way with an astonishing memory to the end. Generous to people who criticised him, he quietly stood his ground, recognising that valid debate is integral to scientific discovery. And, like many another innovative scientist, it is in this way that he triumphed over sceptical adversity to leave a legacy in pioneering the successful treatment of PKU.

At Louis' request there was no funeral and in lieu of flowers he asked that people might make a donation to **CARE, Canada**. ■

Kate Hall

Industry Insights: April 2021

Doris-Ann Williams, Chief Executive, BIVDA

I don't think everyone in Pathology has been given enough thanks for all the hard work you do normally, let alone under the challenging circumstances of the past year, so thank you! However, as we are all aware, the focus on people contracting COVID-19 has meant a reduction in routine appointments from people with long-term conditions or those who have worrying symptoms but were either concerned about overloading the NHS or were frightened of catching coronavirus.

BIVDA do a 6 monthly audit of sales, as part of a European market surveillance activity. We now have figures for 2020 which confirm these suspicions and I've put some interesting results in the table as examples. Unsurprising, and many analytes showed no change in usage, while clearly any related to COVID-19 were dramatically increased. I guess the lack of social interaction was the reason for the dramatic drop in chlamydia tests!

So as part of raising awareness for diagnostic testing, and also to play a role in encouraging the general population to go back to looking after their health, BIVDA have launched a campaign, **Don't Wait; Act.** Something similar has been going on within the Pathology community in Australia which some of you may have seen on Facebook and we are hoping to get partners involved from healthcare professional bodies and patient associations, including the ACB. We've developed a suite of graphics using friendly and relaxed cartoon figures for this and we've included a couple of these here to show you.

Meanwhile, keep up the great work you all do and the end of the pandemic does finally seem to be in sight – as I wrote this I was getting ready to have my first COVID-19 vaccination and can't wait to get down to a beach to walk my dogs!

Test	Percentage drop from 2019
Anaemia	29%
Thyroid tests	14%
Bone & mineral metabolism	14%
Cholesterol	16%
Chlamydia	90%
Autoimmune disease	11%
Allergy	24%
Haematology	9%
Tumour markers	14%

Cartoon formats were chosen for our media message in Don't Wait; Act and we have 15 different scenarios created showing confident and happy people with a variety of healthcare professionals, including a laboratory focussed image. These will be going out via Twitter, LinkedIn and Facebook, and partner organisations will be able to take these and tailor the wording to their own messaging. We will also be adding blogs and information onto a dedicated part of our website through the URL **www.dontwaitact.co.uk** and using **#DontWaitAct**. The aim of the campaign is to add the voice of BIVDA to the others already reassuring the population about healthcare and also to keep an awareness of the important role of diagnostic testing in managing health and staying well. ■

ACB News Crossword

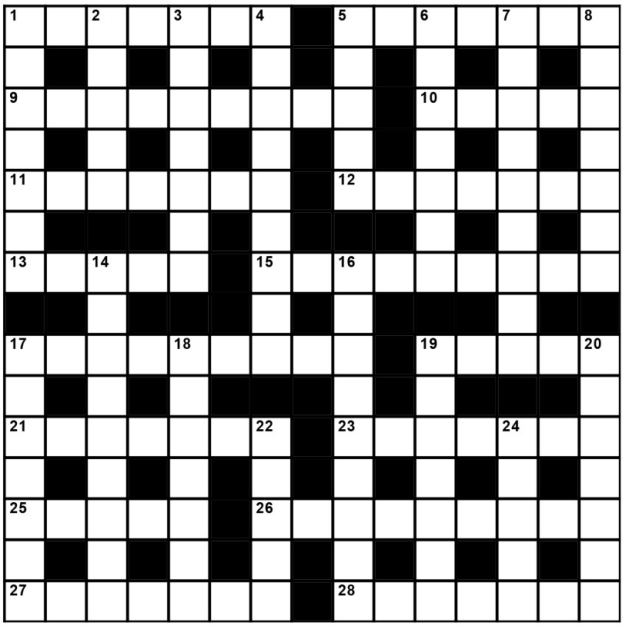
Set by Rugosa

Across

1 Unconscious assimilation of some great cosmos issues (7)
5 For a protein, lab turn around time short, short! (7)
9 Doctor ordered cure-all of very small independent chemical unit (9)
10 Right or due in British law and right in French (5)
11 Surprisingly unemotional, no moan, after a game touch and go decision (4-3)
12 Tale about a falling in love not failing (7)
13 Leading Welsh border golf club (5)
15 Baffling physico-chemical description (9)
17 Hormone store gone, used (9)
19 Shot-in-the-arm from first transaction with new coin (5)
21 Run of the mill unreliable travel agencies lose clients (7)
23 Transport needed to work for biochemical, perhaps from 17 down (7)
25 Become hardened to urine problem (5)
26 Laboratory method of the recalcitrant traditionalist – no dials! (9)
27 New carpets are 4 light for a colourful display (7)
28 Accept grant (7)

Down

1 Never inert, mothers-in-law organised resistance to current rule (4,3)
2 Fruit cocktail Uncle Tom cut out (5)
3 Student's first course about carbohydrate (7)
4 Betraying secret sharing of crime proceeds (9)
5 Professional in an outfit for protection (5)
6 Believed lacking energy, confused mean plague (7)
7 Put out by damaged muscle, setter's duck batting followed good full toss (9)
8 A salt treatment of fever that recurs every other day (7)
14 State of low credit: result, tied purse (9)
16 Mock unusual tiny chest (9)
17 Organs love changes (7)
18 Enter silver amalgam used in reaction (7)
19 Get out, retreating over land with military value (7)
20 Purge corrupt credentials, remove dirt (7)
22 Complex traumas: more admitted (5)
24 Compound verse about team (5)



Solution for February Crossword

ACB News

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