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PENICILLIN

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THE BIOMEDICAL SCIENTIST

THEBIOMEDICALSCIENTIST.NET

OCTOBER 2018

Two years after the end of the most widespread epidemic in history and with a new outbreak raging in East Africa, what can we learn from those on the frontline?

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Redactive Publishing Ltd
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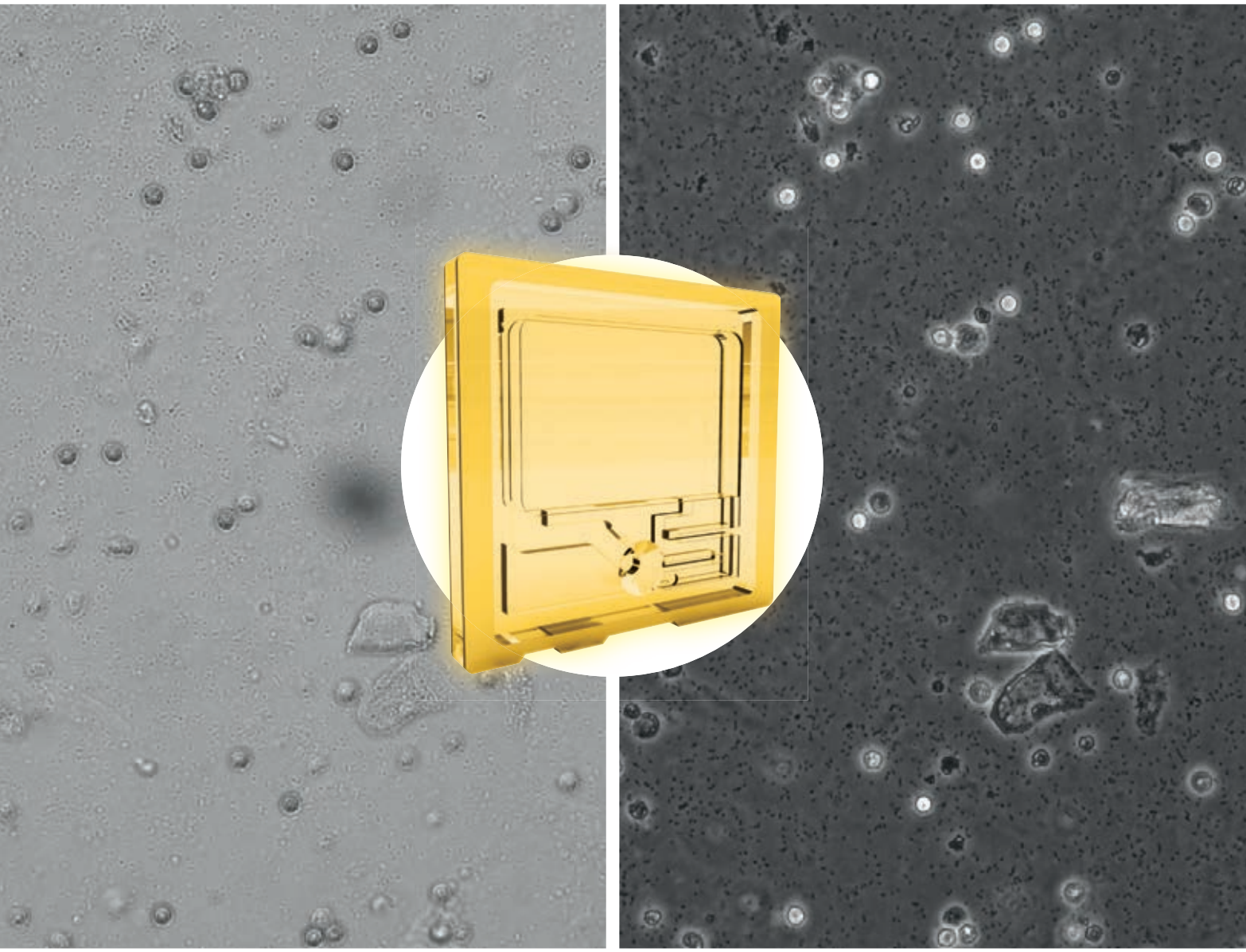

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RITES OF PASSAGE

Have we become so focussed on efficiencies that we no longer know how to celebrate?

I have been fascinated and uplifted, in equal parts, by Grayson Perry's recent Channel 4 series on rites of passage. I envy his artist's gift to see and empathise and then to translate that understanding into something visible and beautiful. In the series he examined our major life events of birth, coming of age, marriage and death and sought to recognise their significance in an increasingly secular society.

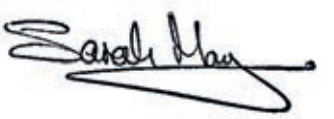
I found his gentle, respectful examination of how other cultures mark major life events reassuring and I felt sad that we seem to have somehow sleepwalked in to the instantaneous selfie world of "take a picture" and then move on. I've never fully understood the national outpouring of grief, bordering on hysteria, when Princess Diana died, but perhaps it was a collective deep-seated reaction to an event that needed to be marked with real feeling and emotion and not a purely ceremonial rationalisation of a death.

Thinking further about major life events, there are many others that do not have roots in religious ceremony but nevertheless are significant landmarks such as graduation and first job. I think that our society has become too adept at boiling things down to the lowest common denominator, or just an excuse for a drink.

In this edition of *The Biomedical Scientist* our Here to Help article is on first day placement nerves. Nothing can fully prepare a person for laboratory life; it is so remote from an evening supermarket job or holiday work in a sports club. To the uninitiated, a laboratory is a high octane, technologically alien environment and the successful completion of a placement, or period of training, is a rite of passage in every sense of the word.

At the other end of the scale, candidates who recently passed the histopathology reporting examination attended an RCPath ceremony to receive their certificates and mark their rite of passage in to a new professional era. It was a moment of shared pride and celebration and that was the essence of Grayson's series: the construction of rites as a vehicle for the coming together and sharing of a celebration.

Our profession has a series of hurdles and rites that mark our professional progress, from registration through to consultant level practice. We are not a profession that does fanfares but I think we are missing a trick if we downplay our milestone successes and I wonder whether we have become so focussed on efficiencies that we have unwittingly lost sight of the importance of the shared celebration of achievement. We have earned our right to recognition, perhaps it's now time to recognise the importance of our rites.



Sarah May
Deputy Chief Executive

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Day 1

- **Hb A_2 Standardisation: Where to Next?**
  Barbara De la Salle, PhD, Director, UK NEQAS Haematology
- **Haemoglobin Variant Identification by Tandem Mass Spectrometry**
  Jason Eyre, Lead Biomedical Scientist, Haemolysis Laboratory, Sheffield Teaching Hospitals NHS trust
- **Established and Novel Applications of vWF Multimer Analysis in the Haemostasis Laboratory**
  Stephen MacDonald FRCPath MPhil, Principal Clinical Scientist, The Specialist Haemostasis Unit, Cambridge University Hospitals NHSFT
- **Changing from HPLC to Capillary Electrophoresis – The Edinburgh Experience**
  Patricia Ryan, BMS Team Leader, Royal Infirmary of Edinburgh, NHS Lothian

Day 2

- **Evaluation of the Sebia Free Light Chain ELISA: Method Comparison with the Serum FreeLite Assay for the Investigation and Monitoring of Monoclonal Gammopathy**
  Melissa Blaylock, Biomedical Scientist, Immunology, Carlisle
- **The Importance of Earlier Diagnosis for all and the Future Landscape of Myeloma Treatments**
  Rosemarie Finley, CEO of Myeloma UK
- **When is a Band not a Paraprotein?**
  Dr Joanna Sheldon, St Georges Hospital, London
- **Protein Quiz**
  Dr Joanna Sheldon, St Georges Hospital, London
- **Round Table Sessions; Small Expert Led Groups for in Depth Discussion**

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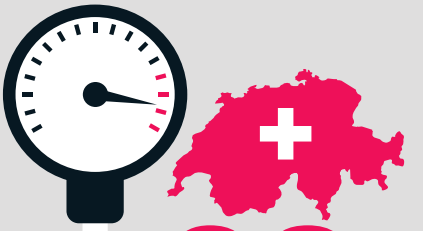
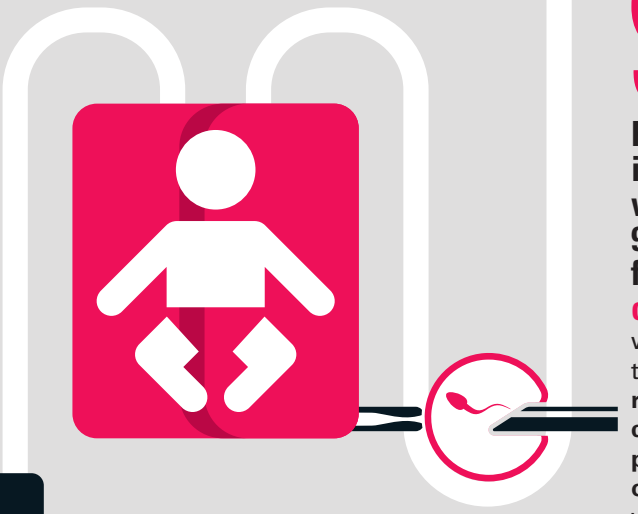
SCIENCE NEWS
IN NUMBERS



Test tube babies

Children born through IVF are six times more likely to suffer high blood pressure than naturally conceived children, says a new study.



96

Researchers in Switzerland who studied 96 teenagers found that one in seven who were **born** through **assisted reproduction** had **clinically high blood pressure by the age of 16**, compared with just **2.3% of those born naturally.**

20,000

Around 20,000 babies are born through IVF in Britain each year.

40YRS

The oldest test-tube baby, **Louise Brown**, is only **40 years old**, which means that the **long-term impact of fertility treatment is still unknown**.

51%

Half of those in England sent a home-testing kit for bowel cancer in 2015 did not use it.

The figure comes from research published in the ***European Journal of Cancer***. In **2015**, only **49% of people aged 60-64** who received a home test kit for the first time returned their samples, **down from 53% in 2010**.

4,383

Male suicide rate lowest in 30 years

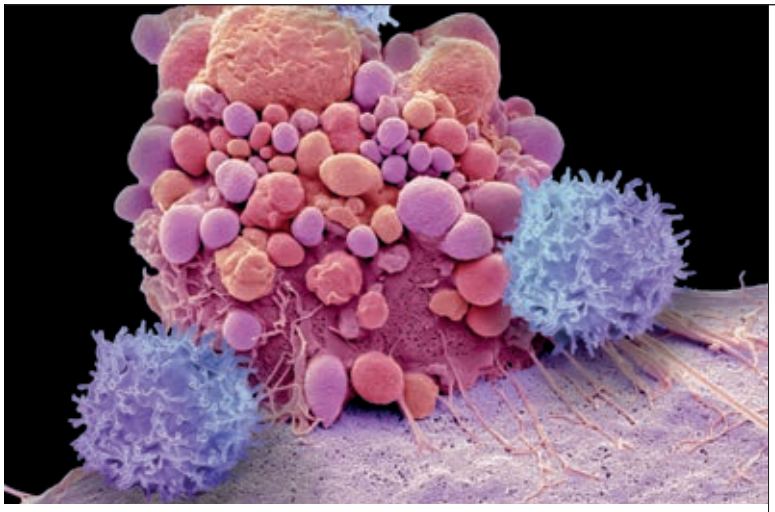
In 2017, there were 4,383 male suicides and the rate was 15.5 per 100,000 men.

This is a **fall from 20 per 100,000 men in the late 1980s**, shows data from the Office for National Statistics.

1.4bn at risk

A global total of 1.4bn people are not doing enough physical exercise, according to a new WHO report.

It says that **one in four people is at risk of health problems due** to a **lack of physical exercise**. Researchers looked at self-reported data on activity from **358 population-based surveys** in **168 countries**.



SCIENCE NEWS

CANCER DRUGS FUND

New leukaemia treatment for children

The NHS will be able to offer children a new cancer therapy labelled the " most exciting treatment advance for decades".

CAR-T is for aggressive leukaemia and can be used when other drugs have failed.

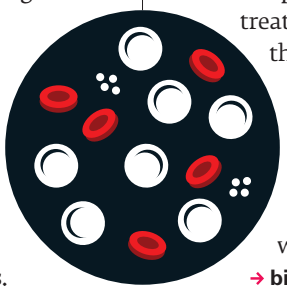
It typically costs hundreds of thousands of pounds per patient.

NHS England boss Simon Stevens says a fair and affordable price has been reached with manufacturer Novartis.

Hospitals could start giving it to a small number of children within weeks. The first three NHS hospitals to apply to use the CAR-T (which stands for "chimeric antigen receptor T-cell") therapy are in London, Manchester and Newcastle.

The CAR-T treatment from Novartis has a list price of £282,000 per patient, though the actual figure NHS England will pay for it has not been disclosed.

The funding will come from the Cancer Drugs Fund, which aims to fast-track access to the most promising new cancer treatments.



HUNTER SYNDROME

EARLY RESULTS FOR GENE EDITING STUDY

Early, partial results from a historic gene editing study indicate that the treatment may be safe and having at least some of its hoped-for effect.

However, it is too soon to know whether it will ultimately succeed.

The results, announced in September, are from the first human test of gene editing in the body – an attempt to permanently change someone's DNA to cure a disease.

In this case, they are tackling a genetic disorder called Hunter syndrome that often kills people in their teens.

In two patients who got a medium dose of the treatment, urine levels of large sugar compounds that are hallmarks of Hunter syndrome had fallen by half, on average, four months later – a possible sign the treatment is working.

Two others who got a low dose have seen little change in these sugars so far.

However, there's no way to know yet whether the change are due to the gene editing.

→ **bit.ly/BS_OctNews02**

COLORECTAL CANCER

LIQUID BIOPSY AND MATHEMATICAL MODELLING

An evolutionary model utilising serial blood samples from patients with advanced colorectal cancer treated with anti-EGFR therapies in a phase II trial could predict personalised waiting time for progression.

The claim comes in a paper in *Cancer Discovery – a journal of the American Association for Cancer Research*.

Study author Andrea Sottoriva said: "By combining frequent longitudinal sampling of cell-free DNA with mathematical modelling of tumour evolution, we were able to make statistical predictions of patients who were at risk of progression.

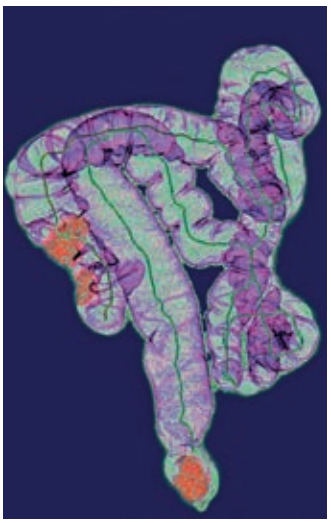
"We could also determine when a cancer was going to come back, on a patient-by-patient basis. This is the first time that quantitative forecasting of this sort has been successfully used in cancer."

The model utilising CEA measurements was applied to six patients to predict time to clinical progression. Of these predictions, three were within 10% of progression time as measured by RECIST.

Predictions generated with high sensitivity cfDNA profiling allowed for the prediction of progression time several weeks in advance, compared with models utilising CEA.

Information garnered from the cfDNA, can be used to generate multiple models based on the predicted growth of individual subclones driven by different mutations.

→ **bit.ly/BS_OctNews01**



IMAGES: SCIENCE PHOTO LIBRARY/ISTOCK/SHUTTERSTOCK

CARDIOVASCULAR DISEASE

PUBLIC URGED TO TAKE HEART AGE TEST

Public Health England (PHE) is calling for adults across the country to take a free, online Heart Age Test, which will provide an immediate estimation of their "heart age".

If someone's heart age is higher than their actual age, they are at an increased risk of having a heart attack or stroke.

Cardiovascular disease (CVD), with stroke and heart attack being the most common examples, is the leading cause of death for men and the second leading cause of death for women.

A quarter (24,000) of CVD deaths are in people under the age of 75, with 80% of these preventable, if people made lifestyle and behaviour changes to improve their heart health.

Knowing their heart age helps people to find out whether they are at risk and consider what they can do to reduce this risk.

Matt Kearney, National Clinical Director for Cardiovascular Disease Prevention at NHS England, said: "The heart age test is a simple and effective online device with the potential to help millions of people.

"The long-term plan for the NHS will prioritise saving lives through improved protection against cardiovascular disease, and increased public understanding of the risks of stroke and heart disease will mean fewer people have to face these devastating conditions."

→ **bit.ly/BS_OctNews03**

24,000

THE NUMBER **OF CVD DEATHS** IN PEOPLE **UNDER 75, 80%** OF WHICH ARE **PREVENTABLE** IF PEOPLE MAKE **LIFESTYLE AND BEHAVIOUR CHANGES** TO IMPROVE **HEART HEALTH**.

WHAT'S HOT AND WHAT'S NOT

HOT

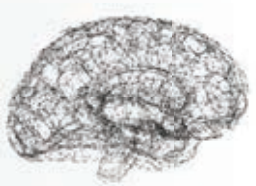
MARMOSETS

Marmosets are an effective research model for Parkinson's disease, as they can mimic the changes in circadian rhythm and cognitive impairment that people have as the disease develops, says a study.

HOT

ARTIFICIAL INTELLIGENCE

A model developed using AI is better at predicting risk of death in patients with heart disease than models designed by medical experts, shows Francis Crick Institute research.



HOT

SHERPAS

A study being conducted into what makes native Sherpas better suited to life at high altitude could help aid intensive care treatment, it is claimed.

NOT

DONALD TRUMP

The increase in death rates due to alcohol, drugs, and suicide is 2.5 times higher in counties where Republicans made gains in 2016, compared with counties where Democrats made gains.

NOT

LISTERIA

The food-poisoning bug Listeria has been shown to respond to the antibiotic fosfomycin, even though the bacteria carry genes that should make it highly resistant.

NOT

BEING SINGLE

A new meta-analysis from the Institute for Biomedicine of Aging says those aged over 65 years old are more likely to suffer from malnutrition if they are not married.

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PUBLIC DISCUSSION

Embedding genomics in the NHS

Genomics England is beginning a dialogue to explore public aspirations, concerns and expectations about the development of genomics and genomic medicine in the UK.

It will bring up to 100 members of the public together with clinicians, academics and industry figures to discuss in depth the science and issues of genomic medicine.

This dialogue takes place at an important time for the 100,000 Genomes Project – by the end of this year, the project will have sequenced 100,000 genomes from 70,000 NHS patients affected by a rare disease or cancer.

The ambition is then to embed genomic medicine into the NHS, so that it becomes part of routine care and treatment, so that everyone can benefit.

The project will last for eight months, and includes a rapid literature review, a stakeholder workshop and public dialogue workshops.

An oversight group will bring independent scrutiny to the project.

Chairing the oversight group is Dr Anna Middleton, Head of the Society and Ethics Research Group at the Wellcome Genome Campus in Cambridge.

She said: "We know that general public awareness and understanding about genomic medicine is quite low. But what I want us to gain through this dialogue is a picture of what public expectations might be, and in particular what patients using the NHS think they should offer in return for their healthcare – their side of this 'social contract'."

→ **bit.ly/BS_OctNews04**

ANTIBIOTIC RESISTANCE

"SUPERBUG SPREADING UNDETECTED"

A superbug resistant to all known antibiotics is spreading undetected through hospital wards across the world, it is claimed.

Researchers at the University of Melbourne discovered three variants of the multidrug-resistant bug in samples from 10 countries, including strains in Europe that cannot be reliably tamed by any drug currently on the market.

Ben Howden, Director of the university's Microbiological Diagnostic Unit Public Health Laboratory, said: "We started with samples in Australia but did a global snapshot and found that it's in many countries and many institutions around the world. It seems to have spread."

The bacteria, known as "*Staphylococcus epidermidis*", is related to the better-known and more deadly MRSA. It's found naturally on human skin and most commonly infects the elderly, or patients who have had prosthetic materials implanted, such as catheters and joint replacements.

The team looked at hundreds of *S. epidermidis* specimens from 78 hospitals worldwide. They found some strains of the bug made small DNA changes that led to resistance to the most common antibiotics.

→ **go.nature.com/2MsEq3g**

UNDER THE MICROSCOPE

This month: hypothyroidism

So, what is hypothyroidism?
Also called underactive thyroid, it is a disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone. Common signs of the condition are tiredness and weight gain.

What causes it?
Either the immune system attacking the thyroid gland, or damage to the thyroid that occurs during some treatments for an overactive thyroid or thyroid cancer.

How can you avoid it?
There's no way to prevent it. However, it can be treated by taking daily hormone tablets to replace the hormones the thyroid isn't making.

Why talk about it now?
A new article in the journal *Mayo Clinic Proceedings* claims that Lisa del Giocondo was suffering from hyperthyodism.

Who is she?
An Italian noblewoman, wife of a wealthy Florentine silk merchant and (more importantly) the model who posed for Leonardo da Vinci's iconic painting the Mona Lisa.

Wait a minute, I thought she suffered from familial hyperlipidemia and premature atherosclerosis!
You are not alone in these thoughts. Research by rheumatologists and endocrinologists published in 2004 also suggested that this was the case, citing visible skin legions and hand swelling as the evidence.

Why the new theory?
Hypothyroidism is thought to be a more likely diagnosis, given that Lisa del Giocondo lived to be 63. Had she suffered from heart disease and a lipid disorder, it's unlikely she would have lived to such an advanced age, given the limited treatments in 16th century Italy.

Why do the Mona Lisa's eyes follow you around the room?
Da Vinci was a very good painter.

IMAGES: ISTOCK

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TECH NEWS

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CliniSys' Pathology Relationship Management (PRM) solution has been specifically designed to support healthcare professionals and the business of pathology.

By combining clinical and business data, the pathology laboratory is able to deliver a holistic profile of every user of the service.

Personalising the pathology experience for all service users is vital to develop relationships and promote customer growth and retention, said CliniSys.

Its PRM enables laboratories to organise all clinical, financial, business and client data centrally in "relationship profiles" to improve communication and collaboration.

→ **clinisys.co.uk**

BRADY CORPORATION

STERILISATION INDICATING LABELS

Brady Corporation's new sterilisation indicating labels provide users with proof of sterilisation.

They are ideal for a broad range of laboratory processes, including sample tracking, inventory management, general tracking, and glassware or tray identification.

The new B-7425-AC label is a steam sterilisation indicating label, and is developed for use in autoclaves. The label changes colour from white to brown/cocoa when exposed to autoclave conditions at 121°C for 10 minutes, and also displays the word "sterilised". Laboratory specialists will get a clear, visual indication to quickly see which sample containers are sterile.

B-7425-AC sterilisation indicating labels can be printed in any laboratory with professional label printers from Brady.

→ **brady.co.uk**

LAB INNOVATIONS

SUSTAINABLE LABORATORY THEME FOR TRADE SHOW

The Lab Innovations trade show will have a new focus this year on the increasingly important aspect of the "sustainable laboratory".

Taking place on 31 October and 1 November at the NEC, Birmingham, attendees can visit the new sustainable laboratory area to see and discuss the latest developments in environmentally-friendly products.

The sustainable initiatives theme is a core topic running through the agendas in both the Royal Society of Chemistry theatre and the Insights and Innovations theatre.

Visitors to the main exhibition can also discover new environmentally-friendly products and examples of sustainable techniques on exhibitor stands.

Registration for the exhibition is free.

→ **lab-innovations.com**

IMAGE: ISTOCK

THE BIG QUESTION

THIS MONTH WE ASK

"Why aren't more biomedical scientists on hospital management boards?"

Krista De Four

Tissue Sciences Service Delivery Manager
St Thomas' Hospital, London

In my opinion, biomedical scientists, specialist in their knowledge and experience, are needed in the laboratory and not on a management board. However, that said, it is vitally important to have them represented and that the communication channels exist to allow them to have a say in any management decisions.

Currently, in London, there is a shortage of experienced, qualified biomedical scientists, the focus for us is to continue to train and allow for the junior laboratory staff to become specialist biomedical scientists within the department.

We also need to concentrate on the advances in science and look at ways of developing techniques as novel developments take place, especially as molecular therapy develops.

I am quite lucky in that the management team in tissue sciences is made up of managers who were once biomedical scientists.

We also have a number of clinical scientists on the management team, which ensures that specialist areas are also represented. We work to a clinical/operational/scientific model, which allows us to deliver the best test result of the patient.

Biomedical scientists love doing what they do and are vital to the laboratory, they do have a say and are represented on hospital management boards via the management team in order to take science forward in order to provide the best test result for the patient.

IMAGE: IKON

Michaela Lewin

Lead Transfusion Practitioner
Cambridge University Hospitals and Royal Papworth Hospital

I think that, despite drives to improve leadership and the promotion of biomedical science, we still remain one of the most unrecognised areas in healthcare, not only by the public, but also by our fellow health care professionals.

Our high level of qualifications, knowledge and skills continue to be unappreciated, with senior managers still seeing us as "technicians" sitting in hospital basements performing simple scientific tests. Our skills, of course, go far beyond this and have developed alongside modern healthcare to include complex strategical and operational planning, budgeting and application of governance frameworks, which helps render us suitable to sit at higher levels within the organisational management structure.

Running a successful pathology service requires far more than knowing how to use a Bunsen burner – which is how many other health care professionals still imagine we spend our time!

Because of this total lack of appreciation, biomedical scientists get very little opportunity for exposure to senior management roles, particularly to board level. I also suspect many of us may not push ourselves forward because we feel as though we would be ill prepared to fulfil the requirements of such a "prestigious" position.

Other professional groups seem to be gaining momentum at a faster rate than us, however these groups tend to be "clinical". If, when and how we will change this remains to be seen.

Stuart Long

Andrology Service Lead
University Hospitals Birmingham NHS Foundation Trust

Biomedical scientists have a pathway where their careers are almost pre-defined with structured direction, using the portfolio system currently in place with the IBMS. This is often not questioned or deliberated upon by individuals or those external to laboratory medicine. Looking at higher management positions, i.e. board level, they are geared towards being more clinical-based and general operational roles as pre-requisites for application.

Biomedical scientists, often already a lesser known group of experts, will themselves not consider this a route or involvement onto trust management boards, particularly as they may feel they lack knowledge of how a trust operates.

The skills gained from working in biomedical science go beyond those that other areas perceive we have – change control, project management, quality management, business management and equipment procurement, for example.

Leadership courses are often aimed at selected health care professionals, where there is an expectation of understanding the trust's key performance areas and where quality is based on national targets.

We need to participate in being less insular, challenge the existing preconceived notions and be more active in our approach to management. Hopefully, this will begin to showcase the skills that we have and widen interactions with clinical areas that know little of who we are or what we do. One must believe in one's self and break the mould.

WHY PROBIOTICS ARE NO PANACEA

Professor Eran Elinav explains why taking probiotics after a course of antibiotics is most likely a very bad idea.

The gut microbiome has gained ever-accelerating interest in the past decade. Research on the topic has given rise to strings of journals and popular science books, as well as a gamut of probiotic supplements. These little pills containing bacterial strains are sold with the intention of replenishing the microbiome to boost a huge range of associated health outcomes, from mental health to the risk of developing diabetes. The resulting industry was worth about US$40 billion in 2017, predicted to rise by about a third by 2024, according to Global Market Insights.

Despite the huge commercial and clinical interest in probiotics, there are some quite remarkable unanswered questions about how – and whether – they achieve the health outcomes that are claimed. A recent study in the journal *Cell* has now blown several holes in the assumed health benefits of probiotics.

"The probiotic concept may be very interesting and promising, but the reality is that it is a highly controversial field with a lot of papers going back and forth and showing opposite things to one another," says Professor Eran Elinav of the Weizmann Institute of Science in Israel and senior author of the study.

Assumption one

Elinav and his team set out to test several widespread assumptions in the field. The first was that the microbiome found in stool samples is a good general indicator of the microbiome in the gut. If the basic diagnostic tool for assessing the state of someone's microbiome is flawed, the treatments given on the basis of them may well not be the most appropriate.

Elinav's group tested 25 healthy volunteers, directly sampling the microbiome in the lining of their gut via an upper gastrointestinal (GI) tract endoscopy and with a colonoscopy. This was the first in-depth assessment of the human microbiome not just directly in the gut lining, but at different points throughout the digestive tract.

"We were able to show that the stool samples of these individuals were a bad proxy for the gut microbiome, and may lead to inaccurate conclusions," Elinav says.

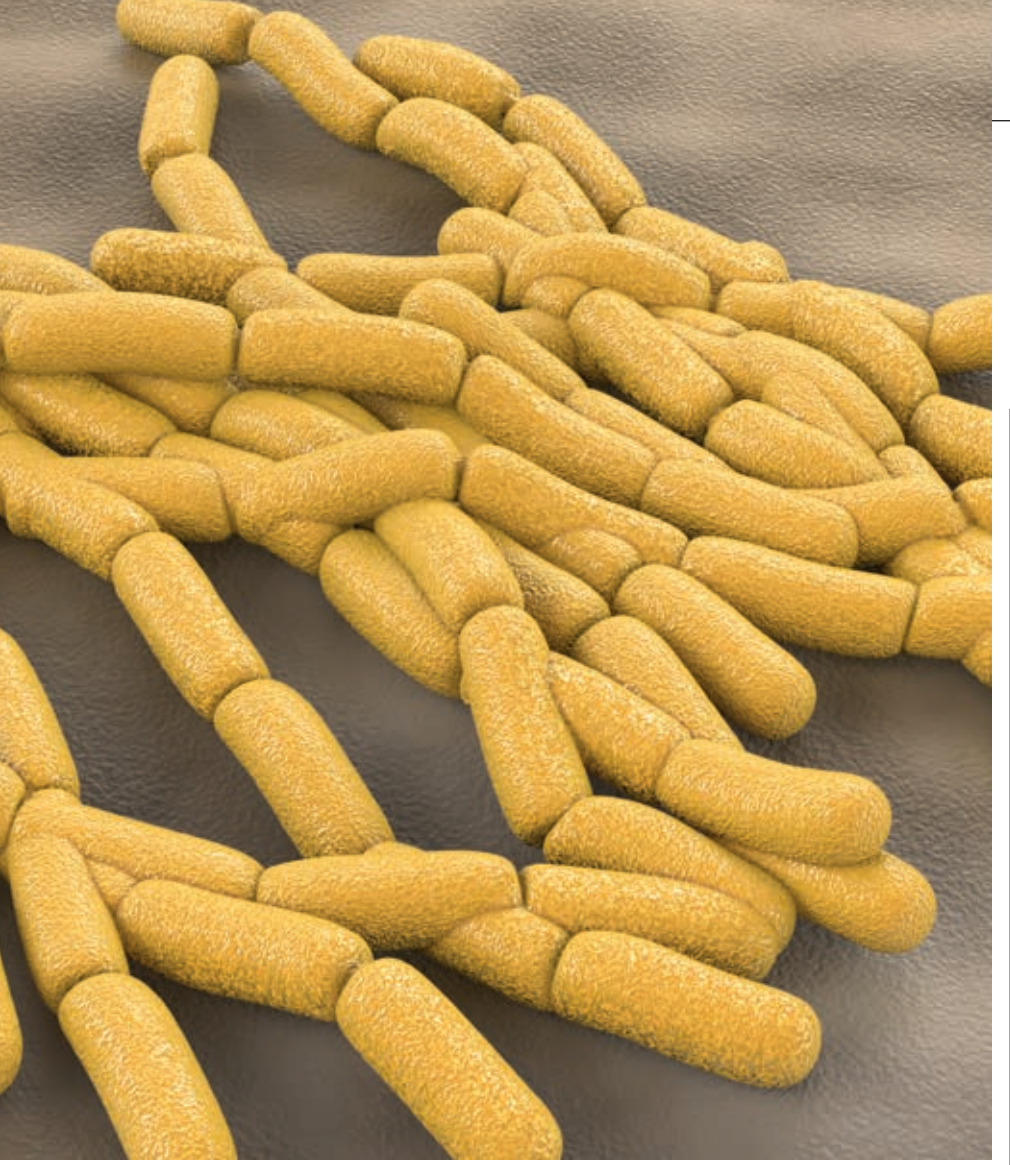
Assumption two

The second assumption put to the test was that taking probiotics changes a person's microbiome. If probiotics are to be used clinically, or bought off-the-shelf by consumers, then it would be reassuring to know that there is an evidence base. A group of 15 volunteers was split between taking a probiotic with common bacterial strains, or a placebo. At three weeks, they all had a colonoscopy and the upper GI tract endoscopy.

"The surprising finding there was that people's colonisation of probiotics is highly, highly individualised and transient," says Elinav. For some, the probiotics simply wouldn't hold. "The probiotics very quickly found their way out the other side." For others, the probiotics colonised their guts thoroughly, having a strong impact on the microbiome and altering theirs own gene expression.

The scientists could predict the reaction that an individual would have. "I can take you and measure your gut microbiome and several key host features and tell you whether you would colonise the tested probiotics or not," Elinav says. This undermines the idea that buying probiotics off the shelf will necessarily do you good.

IMAGES: ISTOCK/WEIZMANN INSTITUTE OF SCIENCE



Assumption three

The third assumption tested relates to one of the most common uses of probiotics – using them after taking antibiotics. A course of antibiotics often kills some of the bacteria in the gut. Countless studies have shown that individuals with an impaired microbiome are more at risk of conditions such as obesity, allergies and inflammation. So, the logic goes, taking probiotics can help replenish the lost microbiome and restore you to health faster.

"This is practised by millions of people, with a widely debated and controversial literature, with probiotic treatments that are not approved by regulatory authorities," says Elinav.

In this part of the study, a group of 21 volunteers took a broad-spectrum antibiotic course for one week. Before and after treatment, the volunteers went through and had the crucial upper GI endoscopy and colonoscopy to sample and assess their microbiome throughout the gut. The group was divided into three: one with no intervention, to see how fast the microbiome recovers without interference.

The second group were given a fecal transplant taken from a stool sample they gave before the antibiotic course. The third group were given a course of probiotics. The idea here was to see what would happen when the large intestine was re-seeded with some of the individual's own bacteria that had been wiped out.

The group that received the probiotics fared the worst. Their microbiome took by far the longest to recover. In fact, five months later, these subjects' microbiomes were still struggling to return to normal.

The study didn't look into whether this group was also experiencing symptoms of poor gut health. However, Elinav suspects they may well be at risk of the conditions associated with post-antibiotic changes to the microbiome. "It seems conclusive that this post-antibiotic alteration is not something that we would want to maintain," he says.

The fecal transplant recipients, on the other hand, did the best. Their microbiomes bounced back to normal within days of the transplant. The no-intervention group also did fairly well, although they took a little longer to restore their microbiomes.

Conclusions

"Probiotic therapy is given to so many people, and yet no one has ever directly assessed what they do in the gut, whether and where they colonise it, and what they do to the indigenous microbiome in the lumen and lining of the gut in a direct measurement," Elinav concluded. "It is truly surprising that this had never been done."

Probiotics may not be the panacea that they are touted to be. Like any other medical treatment, they have potential side-effects as well as benefits. Elinav's research suggests a one-size-fits-all approach to probiotic therapy is not likely to see it fulfil its potential. However, the ability to predict who will and won't respond to probiotics, and in what clinical context it is wise to use them, could open the door to a more promising basis for personalised probiotic therapy. BMS

ALL ABOUT PROBIOTICS

- ✔ Probiotics are live bacteria and yeasts.
- ✔ They're often added to yoghurts or taken as food supplements.
- ✔ They are generally classed as food rather than medicine, which means they don't undergo the rigorous testing that medicines do.
- ✔ There are claims they can prevent or treat digestive disorders, allergic disorders and other conditions.
- ✔ Strong scientific evidence to support specific uses of probiotics for most conditions is lacking.

Two years after the end of the most widespread Ebola epidemic in history and with a new outbreak in East Africa, what can we learn from those on the frontline?

In December 2013, an 18-month old boy called Emile Ouamouno died in the small village of Meliandou in Guinea, West Africa. He had been playing with the bats that lived in a tree stump a few metres from his home. Soon after his death, his sister and mother also died, and within four months the village had buried 14 of its residents.

Scientists have since reported that the bats were infected with Ebola.

But it was not until March 2014, when the virus spread to Liberia and then on to Sierra Leone, Nigeria, Mali and Senegal, that it started to garner global attention.

Fast-forward 21 months and the Ebola epidemic had officially claimed 11,315 lives, but with many deaths going unrecorded, some claimed the figure was up to three times higher.

As well as taking thousands of lives, the epidemic devastated already fragile healthcare systems and ravaged the economies of countries, some of which were still limping back towards recovery after a bloody civil war.

On 13 January 2016, the World Health Organization (WHO) declared the last of the countries affected, Liberia, to be Ebola-free. By this time the epidemic has killed five times more victims than all other know Ebola outbreaks in history combined.

The disease is now back. This time it has hit East Africa. From July to September this year, it claimed 85 lives in Congo and infected a further 39 people. Most of the victims were from villages

PHOTOGRAPHY: RICHARD GLEED

and about 20 were from Beni, a city of several hundred thousand people with close links to Uganda. Then, on September 5, Peter Salama, the WHO's Head of Emergency Operations tweeted: "Ebola case from Beni has died in Butembo, a city with close to 1 million people."

As health officials struggle to control the virus's spread through experimental vaccines and treatments, we hear the first-person accounts of two scientists who were on the frontline in 2014 and one who is involved in the current efforts to stop the East Africa outbreak escalating into another devastating epidemic.

NEIL BENTLEY

Head of Technical Services for the National Infection Service, Public Health England

As part of the 473 volunteer scientists, I deployed to support the Ebola outbreak in West Africa within Sierra Leone between October 2014 and July 2016.

Our remit from the British government was to provide three laboratories with the capability to provide a molecular Ebola and RDT Malaria diagnostic service to support the outbreak. Latterly we also provided basic biochemistry and haematology diagnostics from each of the laboratories. Our laboratories at Kerry Town, Makeni and Port Loko were strategically placed within the Ebola Treatment Centres (ETCs) close to, but outside, large population areas.

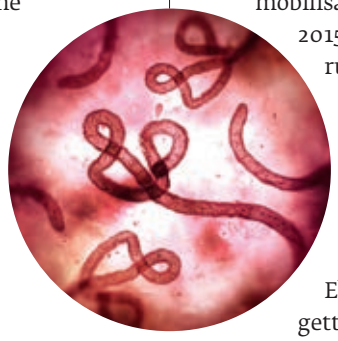
My role was to help develop and lead the operational and technical laboratory service and organise a suitable in-country cold chain supply of reagents and consumables from the UK. Initially, this required us to work with the British military to help design and build the laboratories from scratch. This meant sourcing basic essentials, such as water and electricity, for the laboratories. There was significant pressure to open them as

soon as possible and each initially opened while the ETCs were being built around us.

As the laboratories opened, it quickly became apparent that provision of diagnostic services was only a part of the public health requirements needed. There was also a requirement to train and develop local healthcare and support staff on how to effectively obtain patient samples and transport them to the laboratories as quickly as possible. We embarked on a series of community training and worked with the local transport teams to expedite sample delivery. These steps were particularly important, as any patient with a pyrexia (that can be caused for many reasons) was held within the Ebola holding centres, frequently for up to five days while waiting for laboratory results. Therefore, the probability of cross-infection while in these holding centres was significant. Our training and logistical support helped reduce the turnaround time from days to hours and hopefully significantly reduced disease transmission.

With laboratories, logistics and the public health running smoothly, we changed focus and worked with the Department of International Development, the Sierra Leone Ministry of Health and Sanitation (MOHS), NGOs and other international partners on measures required to control the outbreak. This involved helping with the coordination of laboratory and public activities at the national level, and included assessing viable technologies to help support diagnosis and public health.

My role within Sierra Leone continues, with assisting MOHS on the provision of a sustainable diagnostic laboratory service, and provision of effective public health and emergency response activities. This includes the building and refurbishment of three diagnostic laboratories at Makeni, Bo and in the capital city Freetown.



With personal hindsight, there are many things that we could have done differently. Namely reacting to this outbreak sooner, and by initially providing laboratory services out of tents while the ETC laboratories were being constructed. Locally we used traditional fluid balance and palliative medical techniques supported by state-of-the-art laboratory diagnostic services for the duration of the outbreak. Subsequent vaccine development, Ebola virus disease research and global changes in attitude will hopefully prevent outbreaks on this scale in the future.

Finally, Sierra Leone and its people will always have a special place in my heart, and, having been given an African name "Pa Bumba" (meaning rich old man), I will keep returning to try to make a difference.

VICTORIA ATHERTON

Senior Biomedical Scientist (Microbiology), General Hospital, Jersey.

Due to my day job, I had been following the West Africa Ebola outbreak in 2014 with interest. As a member of the Army Reserve, I was asked to attend a pre-deployment Ebola-specific training course. This was the first indication that I might be mobilised for Operation GRITROCK, I was excited at the possibility and also nervous of the challenges I may face.

In December 2014, I received my mobilisation papers. In January 2015, I left Jersey with a rucksack, kit bag and day sack, containing everything that I might need.

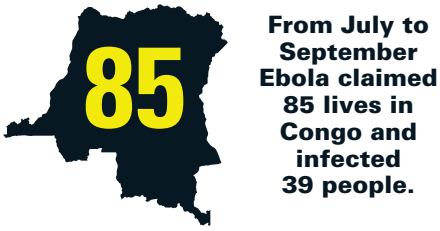
All the deploying Defence Medical Services personnel spent two weeks in York carrying out Ebola-specific training and getting familiar with the protective equipment. The training allowed everyone to get used to working together as a team. We then flew to Sierra Leone. I think we were all apprehensive, but at this stage probably more about our accommodation and the country itself, rather than the job. It was hot and I spent the next two and half months looking slightly pink and very shiny.

The laboratory in Kerry Town was split in two, with our colleagues from Public Health England performing the Ebola testing. The MOD staff performed full blood counts, biochemical profiles and other tests on Ebola-positive samples. The laboratory was near a patient rest area and it was amazing to see those that survived get stronger before being discharged. Survivor ceremonies were performed, which involved a lot of dancing and singing. The defence medical personnel were accommodated at an old army camp, where the food was brilliant and we travelled to work each day in an old school bus. A lot of our free time was spent running and we also had film nights and quizzes.

EBOLA IN NUMBERS

11,315

The 2014-16 Ebola epidemic officially claimed 11,315 lives.



From July to September Ebola claimed 85 lives in Congo and infected 39 people.

Being in Sierra Leone at such a time was an amazing experience, I think we all hoped we had helped to combat a dreadful disease. We made some friends, had some laughs, worked hard and had a small insight into an interesting country with fascinating cultural links to the UK.

CLAUDE BANDELIER

Laboratory Manager, Médecins Sans Frontières

When Médecins Sans Frontières arrived in Mangina, the epicentre of the current Ebola epidemic in North Kivu, Democratic Republic of Congo, the local health centre was already full of confirmed and suspect patients, including many medical personnel who had been infected at work. We had to work quickly to improve the biosecurity of the isolation ward and simultaneously construct an ETC where the patients could be transferred and treated safely. With an initial capacity of 68 beds, the ETC received 37 patients the day it opened.

As a biologist, my role was to construct a secure laboratory inside the ETC in order to carry out biomedical analysis in collaboration with the Congolese Ministry of Health and the National Institute of Biomedical Research. The laboratory, set up under a tent, is equipped with a portable glovebox and is situated on the edge of the high-risk and low-risk zones.

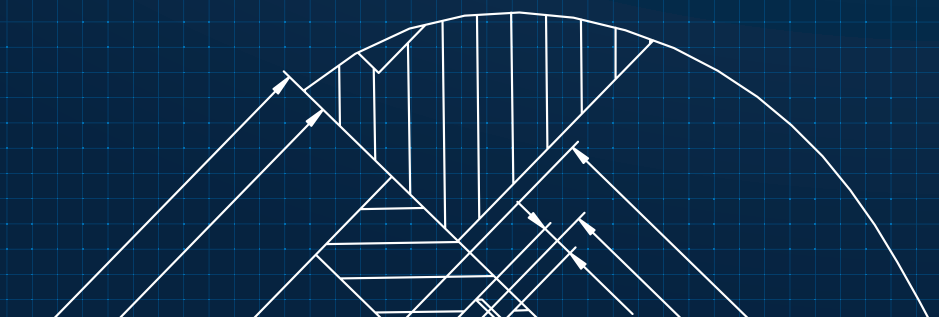
The role of this laboratory is to quickly diagnose on site all suspected Ebola patients on admission to the centre, to be able to isolate the "positive" patients and refer the "negative" patients to a suitable health structure for further care. It also gives us the means to regularly monitor patients' biological parameters in order to help assess their condition and adapt their care accordingly. The laboratory also provides diagnostic support to community health teams who swab the bodies of those suspected of dying of Ebola in the community in order to identify new hot spots of the outbreak.

I have worked with MSF on a previous Ebola outbreak and came to North Kivu to contribute my experience and learn more about Ebola. A difficulty in this epidemic is the geographic location. This time, Ebola has erupted in an area of active conflict between armed groups. Movement between villages and access to certain areas is restricted and difficult. Ebola is very difficult to predict. Constant care and attention is required, and it is difficult to know how the epidemic will evolve. It is very important to work closely and transparently with local people and to earn their trust. They must be informed about the virus and the response in order to accept the presence of international organisations. It is also important that equipment is developed to be more mobile and compatible with the constraints of the field.

With the difficult working conditions that come with an Ebola emergency, in terms of long hours, stress, constraints and emotions, we have also shared good times with the staff and community. Discharging cured patients is always very moving and rewards us for our work. BMS

IMAGES: GETTY/ISTOCK

A BLUEPRINT FOR THE FUTURE



Bill Bartlett and **Paul Hawkins** on transforming NHSScotland's laboratory medicine services.

NHSScotland provides healthcare to a population of approximately 5.3 million people across an area that constitutes a third of the UK land mass. It faces challenges around rising demand and many other drivers for change common to the rest of the UK. These, in combination with a fundamental requirement to deliver better care, better experience of care and better cost of care (triple aim), are driving the need for transformation of services. It follows that underpinning services, such as those provided by laboratories, must also undergo transformation to deliver future requirements of the evolving healthcare system. Given the dependence of patient pathways and outcomes upon laboratory outputs, failure to deliver transformed services that are optimally configured to address both local and national priorities will compromise the value of investment in diagnostics and delivery of the triple aim. New service configurations need to deliver equitability of access, efficiency in delivery, effectiveness in impact, resiliency and sustainability of service and be not least affordable. Taking all these issues into account, a process involving service providers and stakeholders has resulted in the agreement to move forward with the development of a Distributed Service Model (DSM) for laboratory services within NHSScotland. A blueprint and set of guiding principles have been developed to enable the DSM delivery under a new governance structure. This sees the establishment of a Laboratory Oversight Board to facilitate the development of the DSM through new Regional structures. NHS National Services Scotland (NSS) has been tasked by the Scottish Chief Executives group with delivery of a National Laboratories Programme, which has been allocated £6.7m for initial key work to enable the developments.

The current National Laboratories Programme has arisen from work undertaken through the NHSScotland Shared Services Programme (SSP), which was extended to deliver a health portfolio that included laboratories in 2015. In 2016, a small team was established within the SSP Health portfolio tasked to develop the laboratories element. That team worked with the laboratory service providers and other stakeholders through a number of workshops to develop a position paper on laboratory shared services that was presented to NHSScotland chief executives in October 2016. That paper included a detailed PESTEL and SWOT analysis of the current service model and also took into account work undertaken by NHSScotland's managed diagnostics networks presented to the Diagnostic Steering Group in 2015. It resulted in a mandate to move forward to delivery of a strategic paper based on a proposal to develop a DSM for laboratory services in Scotland and to establish a

small number of working groups around information technology, data and innovative technology. The position paper also identified a set of guiding principles to be followed in the development of services to realise the concept of the DSM.

The DSM strategy paper was delivered in July 2017 and with a high-level description of the proposed model emerging through extensive stakeholder engagement. The contention put forward was that stakeholders agreed that there is an opportunity to use the significant resources available to health boards to deliver laboratory services in a way that is more efficient, effective, equitable, resilient and affordable. The DSM concept is one of delivery an optimal service configuration in the various localities across Scotland. The delivery units are to provide the correct volume, range and repertoire of tests reported within an appropriate timescale to meet the needs of the locality and configured as a whole to enable delivery of national priorities in the context of the triple aim. A strategic is delivery of an optimal distribution of laboratory services across Scotland with concentration of workloads and sharing of expertise across wider geographical areas. The concept is one that addresses drivers for change and requires delivery of a functional distribution of service across the system to deliver whole healthcare system value and resilience, rather than de facto centralisation in to reduce costs.

Delivery will depend upon coordination across and between laboratories and standardisation of operating procedures across services. In planning terms, this will equate to a single virtual service functioning to consistent standards across the wider organisations while different aspects of service are delivered by the relevant operational unit at the most appropriate level whether national, regional, health board level, individual hospital or community.

The strategy paper was approved and work subsequently undertaken to develop

DESIRABLE ATTRIBUTES OF NHSSCOTLAND'S FUTURE

"Functional distribution of laboratory resource that enables equitable delivery of high quality health care independent of location"

a full business case presented to CEs in April of 2018. This built on previous work with further input from an IT Group, a Data Group and DSM Design Group. The case reflected the requirement identified to take an incremental approach to the delivery of the DSM, the emerging regionalisation agenda arising from the publication of the Scottish Government's *Health and Social Care Delivery Plan* in 2016 and the need to have a new governance structure to support this agenda and ensure national consistency of service. The case was accepted and funding allocated to a National Laboratories Programme with the following Key deliverables:

- A new governance structure that supports the delivery of a DSM with national consistency
- A National Laboratories Blueprint. Delivering a vision for the laboratory services focusing on process, organisation, technology and information.
- IT Connectivity, with all Scottish laboratories implementing NPex for lab to lab electronic ordering
- Data sharing, through development of a national data platform to support business and clinical intelligence requirements
- A high level specification for LIMS to enable national consistency in a key procurement area

It is important to note that the incremental approach is being taken with the view of achieving short- to medium-term benefits, adding value to laboratory services, while maintaining a clear focus on the longer-term transformational change required to deliver the optimal DSM. The final form of the DSM will ultimately reflect function, meeting the needs of stakeholders, which in turn will be defined by the requirements of NHSScotland's healthcare delivery model evolving in the context of the National Clinical Strategy.

Longer term benefits are anticipated that are both financial and non-financial, in part these will be achieved through the appropriate consolidation of services, facilities and equipment and whole system laboratory service redesign. The business case illustrated the potential benefits of laboratory service transformation with examples from current initiatives in Scotland. It also recognised the fact that delivery of optimised services with appropriate allocation of resources has the potential to deliver significant downstream benefits to overall healthcare delivery and the potential to address current risks (e.g. service resilience, requirement for investment in new technologies). Clearly there is a drive for change to address the issues of variation and waste within the current system, but this should be seen as an opportunity to identify resource to invest in developments that increase the effectiveness and value of the allocated resource envelope. Developments in technology, information and knowledge

management, artificial intelligence, the medical evidence base and the emergence of new modes of practice will challenge the delivery model and potentially enhance the value of redesigned services.

The scale and complexity of the task to be undertaken to deliver the DSM should not be underestimated. NHSScotland's clinical laboratory services are currently provided by 14 territorial and two special health boards (Scottish National Blood Transfusion Service, Golden Jubilee National Hospital) and have a projected spend of £1.5b pounds over the next five years. Focusing on the territorial boards, it is estimated that over 3,800 full-time equivalent staff are directly involved in service delivery across 27 sites out of 87 laboratories. In addition, total NHS service provision also includes a number of national services commissioned by NSS; there is therefore a considerable resource managed and applied thorough a complex model with multiple stakeholders involved in service provision and usage. Following the publication of the *Health and Social Care Delivery Plan*, the territorial Boards have been allocated to three regions for the purposes of planning:

North Region	East Region	West Region
NHSGrampian	NHSBorders	NHSAyrshire & Arran
NHSHighland	NHSFife	NHSDumfries and Galloway
NHSOrkney	NHSLothian	NHSForth Valley
NHSShetland		HHSGreater Glasgow & Clyde
NHSTayside		NHSLanarkshire
NHSWestern Isles		

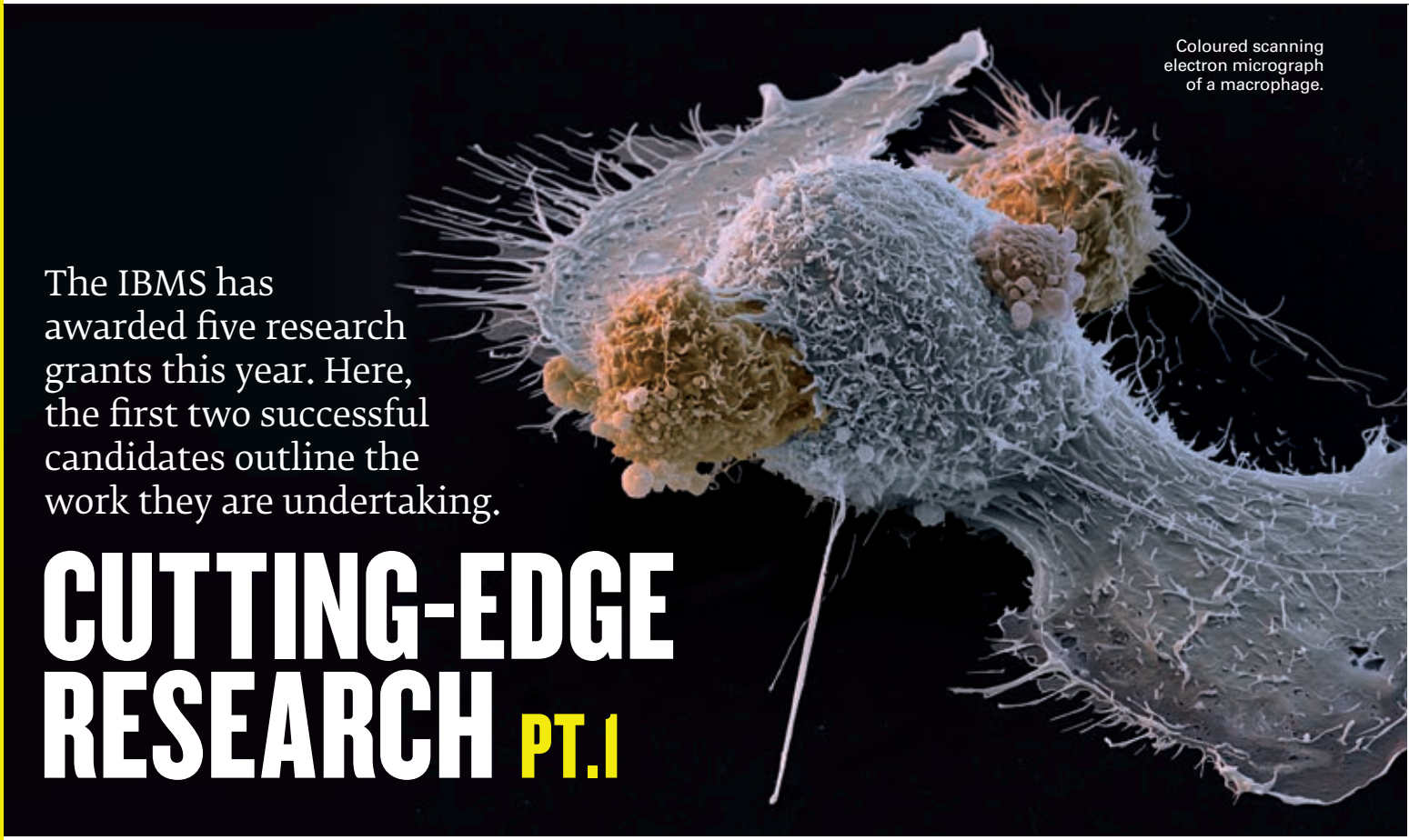
The scale and complexity of the task to deliver the DSM should not be underestimated

The governance structure for the delivery of the DSM will be delivered via the formation of operational boards for laboratories in each of the three Regional structures feeding into a Laboratories Oversight Board (LOB). Those regional boards are seeking delegated authority from there constituent health boards to enable change. The LOB has a membership that enables input from regional, national and partnership perspectives and is chaired by Paul Hawkins the NHS CE for NHS Fife. Included within the LOBs remit and purpose is the responsibility for aligning national and regional plans for laboratories transformational change and ensuring that the Laboratories programme aligns to the strategic direction of NHS Scotland. The latter will be enabled by the availability of the national laboratories blueprint. At the first meeting of the LOB it was agreed that the blueprint and guiding principles for the DSM should be embedded within the terms of reference of the Regional Operational Boards to enable delivery of a vision for services across NHSScotland shared and thus consistent.

The National Laboratories Blueprint (NLB) attempts to capture the here and now of the current laboratory services model, identifies the steps that need to be taken to deliver the desired future model for laboratory services and identifies the desired endpoints to be delivered by the DSM. It supports an incremental approach to transformation that, if adopted, will enable delivery of the national strategy for laboratories and progression towards a DSM that will meet NHSScotland's needs today and in the future.

The current focus on laboratories in Scotland presents both a challenges and opportunity for those providing services. The approach has delivered a clear vision for the future of services that necessitates service transformation. This clearly delivers challenge the old order of things. The drivers for change impacting on the current service model are increasing in number and severity and drive the need for the transformation. Not all are adverse. The availability of new technologies and new approaches to service delivery that support new ways of working provide new opportunities for all working in laboratories. In addition, the approach being taken to transformation in Scotland recognises the value of diagnostics in healthcare and has at its core a focus on value and not cost with a key focus being the triple aim. This is being increasingly recognised and is a positive for those proposing service developments. The combination of the DSM blueprint, the guiding principles, the new governance structures, increased understanding of the value of diagnostics in healthcare and the adoption of an incremental approach to change towards an optimal delivery model provides massive opportunities for the future of laboratory diagnostics in Scotland. BMS

Dr Bill Bartlett is Clinical Lead National Laboratories Programme NHS National Services Scotland. **Paul Hawkins** is Chief Executive NHSFife and Chair of the Laboratories Oversight Board.



Coloured scanning electron micrograph of a macrophage.

The IBMS has awarded five research grants this year. Here, the first two successful candidates outline the work they are undertaking.

CUTTING-EDGE RESEARCH PT.1

José Ignacio Saldaña

Lecturer in Immunology, University of East London

Antibody crosslinking of the cell surface receptor Siglec-F: a method to study alveolar macrophage function and adaptation

Macrophages are highly diverse immune cells that carry out functions that are specialised to the characteristics of the tissue in which they exist.

As these cells move in, they experience a process of adaptation driven by signals provided by local factors and by the physiological environment. Therefore, macrophages of the airways (alveolar macrophages), liver (Kupffer cells) and brain (microglia) have very different roles and can be differentiated from one another.

Lung tissue is delicate and constantly exposed to particles, dust and pathogens contained in the air. Upon detection of pathogens, alveolar macrophages are quick to respond to protect the airways, being highly pro-inflammatory. These cells are kept under a regulated state thanks to close contact with epithelial cells that provide negative controlling signals through specific cell surface proteins. This regulatory communication system is essential, as any unwanted inflammation can damage the delicate lung tissue or induce scarring and remodelling, leading to loss of function.

Other proteins (e.g. mucins and collectins) are ubiquitous components of the extracellular matrix of the lung that also deliver developmental and regulatory signals to alveolar macrophages through receptors such as Siglec-8 and its mouse counterpart Siglec-F. The specific role of Siglec-F, as a regulator of the process of macrophage function and adaptation to tissue microenvironments, is not fully understood. Therefore, targeting and modulating signalling through Siglecs has the potential to create new specialised therapies.

Dr Saldaña's IBMS Research Grant-funded project aims to target Siglec-F and uncover the potential effects this could have on resident lung macrophages, function and tissue adaptation.

Thomas McDonnell

Research Associate, University College London

Common pathways in systemic lupus erythematosus and antiphospholipid syndrome

Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are autoimmune disorders characterised by autoantibodies, activation of inflammatory and coagulation pathways and an adverse impact on quality of life. Characterised by thrombosis, strokes and/or recurrent pregnancy loss caused by antiphospholipid antibodies (aPL), APS may occur alone or in combination with SLE. Systemic lupus erythematosus is a multisystem disease with potentially serious organ and life-threatening manifestations in which anti-dsDNA antibodies fluctuate with disease activity. Despite the clinical severity of these diseases, treatments are imperfect and lack specificity against autoantibodies.

Approximately 40% of APS and SLE patients develop antibodies to serine proteases, principally factor Xa (FXa)

IMAGES: SCIENCE PHOTO LIBRARY

and/or thrombin (Thr). The relevance of these antibodies to disease is currently unknown. As both FXa and Thr are therapeutic targets in other disorders and coordinate interactions between complement and coagulation cascades, it is tempting to speculate that antibodies directed against these factors may be important in SLE and APS.

Both the coagulation and complement pathways are proteolytic cascades of serine proteases and are activated in both diseases. In SLE, complement consumption is a biomarker of disease flares, and low C3 levels are associated with active disease. In APS, complement activation is associated with pregnancy morbidity and the generation of thrombosis in mouse models.

Interactions between coagulation and complement cascades are poorly characterised. FXa and Thr have been shown to cleave complement factor 3 (C3) and 5 (C5) that are central to complement activation; however, the precise function of antibodies to FXa and Thr are unknown and Dr McDonnell hypothesises that they promote complement activation in patients with SLE and/or APS.

After consultation with patients, 88% to 90% of 527 respondents felt this work was important and relevant to management of these diseases, confirming patient/public interest in this mechanistic research evaluating the impact of autoantibodies on FXa-and Thr-mediated complement cleavage in SLE and APS.

To determine whether or not these antibodies are associated with complement cleavage in patients, Dr McDonnell looked for clinical correlations between anti-FXa and/or anti-Thr IgG positivity and C3 levels in patients with SLE under long-term follow-up at University College London Hospital. Patients with either anti-FXa and/or anti-Thr IgG positivity were identified and their C3 levels examined from five previous consecutive clinic visits. Significantly, lower levels of C3 were found in patients with both anti-FXa and anti-Thr IgG positivity than with single anti-FXa or anti-Thr IgG positivity.

Dr McDonnell's research has focused on the cleavage of C3. His research grant-funded further study will examine the effects of anti-FXa and anti-Thr antibodies upon FXa- and Thr-mediated C5 cleavage, which is important in the formation of the membrane attack complex that mediates cell lysis. The aims are i) to assess anti-FXa/Thr activity on complement cleavage and AT-mediated inhibition; and ii) develop a system applicable to serine protease-mediated complement generation and cleavage in endothelial cells. BMS

Below. A man pulling off the filter during penicillin manufacture at Glaxo, circa 1956.
Right. New York, 1945. Dave Tarlow, the Manager of Whalen's Drug Store, putting up a sign advertising that they stock penicillin.

THE BIRTH OF MODERN MEDICINE

How an unintentional discovery in a messy lab ushered in a new era for infectious diseases.

Of all the eureka moments in science, one of the most celebrated occurred on the morning of 3 September 1928 when, returning from a holiday in Scotland to his lab at St Mary's Hospital in Paddington, the newly appointed Professor of Bacteriology Alexander Fleming began to sort through the various plates of staphylococcus colonies that he had abandoned two weeks earlier. His attention was drawn to a plate that had been left uncovered. This was not unusual in itself, given Fleming's reputation for keeping an unkempt lab, but what certainly struck him as strange was a contamination of blue-green mould on the plate.

A small piece of matter might have come in through the open window, landed on the plate and started to grow. But odder still, and far more important, was the effect it had created. For while the rest of the plate was a sea of staphylococcus spots, the area around the mould was free of any sign of the bacteria. It was as though some property of the "mould juice", as Fleming called it, was resisting the spread of the staphylococcus. From that moment, from that happy accident, the modern era of the antibiotic flowered.

Fleming and his assistants later identified the mould as "penicillium" and found that it was just as effective against other bacteria, including streptococcus and meningococcus. He was quick to announce his findings in an article in the *British Journal of Experimental Pathology* in 1929, writing: "The staphylococcus colonies became transparent and were obviously undergoing lysis... the broth in

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Petri dish with molds (penicillium, yeast, mucor) isolated on black.

"Fleming is a sort of Christopher Columbus. He says that he has found something, but he doesn't know what it is"

which the mould had been grown at room temperature for one to two weeks had acquired marked inhibitory, bactericidal and bacteriolytic properties to many of the more common pathogenic bacteria."

But while observing the effects of the mould and replicating it to a small degree were one thing, pinning down the vital ingredient and understanding how it worked were quite another. "Fleming discovers what he calls penicillin, but it is just a yellow liquid," says Robert Bud, Research Keeper at the Science Museum and author of the book *Penicillin: Triumph and Tragedy*. "It's not what we know as penicillin at all. The metaphor I have is that Fleming is a sort of Christopher Columbus. He says that he has found something, but he doesn't know what it is."

Halting progress

Part of the problem for Fleming was that, try as he might, the chemistry to properly isolate and grow penicillin in suitable quantities didn't exist in the late 1920s. He also ran into a degree of scepticism, as the lure of a "wonder drug" was not something to easily sway a society that had seen more than enough quack medicine. As a result, Fleming couldn't capitalise on his discovery, and the promise of penicillin and its antibacterial action lay dormant.

Despite the stuttering attempts of Cecil Paine at the Sheffield Royal Infirmary to use penicillin to treat patients with eye infections in 1930, it wasn't until 1939 and the work of a group at the Sir William Dunn School of Pathology at Oxford University that included Howard Florey, Ernst Chain and Norman Heatley that Fleming's findings were successfully revisited. They learnt more about the mould's chemical and therapeutic properties, found how to isolate the key active ingredient, and devised a way to produce penicillin in sufficient quantities to begin formal testing on live subjects.

The equipment was still crude, though, and the onset of World War Two wasn't about to make it any easier. With materials in short supply, they press-ganged every suitable container they could find to hold the solution that would produce the mould – milk churns, bell jars, bath tubs and even bed pans.

It worked well enough, and in 1940 the team carried out its first experiments on mice infected with streptococcus. The rodents left to their own devices died, while those injected with penicillin survived. Emboldened by their success, the team began looking for a suitable human subject. They found it in the shape of Albert Alexander, a police constable hospitalised at the Radcliffe Infirmary in Oxford. A rose thorn had scratched his face and the wound had become infected with staphylococcus and streptococcus, causing severe abscesses on his face, eyes, scalp and lungs. Having done all they could, the doctors accepted an offer of help from Florey and his team.

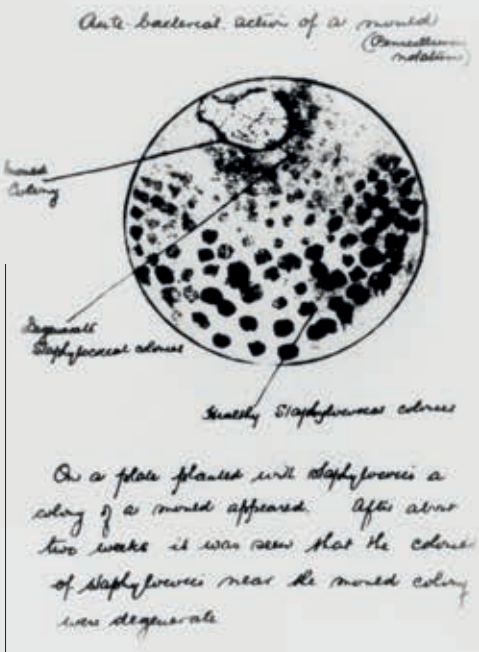
They moved in and immediately set about injecting Alexander with penicillin. Before long, and to everybody's astonishment, he showed signs of recovering. His abscesses started to heal and he was even well enough to eat. But after just five days the team exhausted its meagre supply of the drug, and it hadn't been enough to kill off the infection completely. Alexander's condition deteriorated and this time there was no saving him.

Moving abroad

The wartime shortages and regulations were hampering the team's efforts to produce a more workable form of penicillin, and so they began to look across the Atlantic for help – Florey in particular had good connections in the US. But there was more to it than just a lack of resources, says Robert Bud: "Another fundamental issue is the technology of fermentation. It requires a lot of surplus organic material, which is what the Americans have. Corn starch, maize and so on. Not only would the British have had to import this, a tall order at that point in the war, they no particular expertise in fermentation."

Foley found what they needed at the US government's Northern Regional Research Laboratory (NRRL). It had set up operations in Peoria, Illinois, in the heart of the American midwest, where the required organic material was abundant. It also had a specialist fermentation division that had been developing extensive expertise in the technology since the end of the First World War.

Working with the Oxford team, the NRRL fermentation division began to



Left. Notes on a drawing of the culture plate of the fungus Penicillium notatum, by Fleming.
Below. Fleming studying mould cultures in his laboratory.

apply all its skill and experience to the job of boosting the production of penicillin to the sort of industrial levels that would make the wonder drug more viable – thousands of litres of solution were needed to create enough to treat just a single infection.

This broke down into three key tasks: improve the submerged fermentation technique, devise a way to speed up the growth of the mould, and find a strain of penicillin that would deliver higher yields.

Perfecting the process

NRRL had been using a patented fermentation process since the mid 1930s, where they grew the mould submerged in the solution rather than just on the surface of the containers. Whereas the fermenting process had been restricted to Fleming's meagre plates in 1928 and the Oxford group's improvised bath tubs in 1939 and 1940, it was now taking place in high-capacity rotating drums and vats, both of which could feed vital oxygen into the medium without breaking up and destroying the mould.

The next step was to substitute the Oxford team's brewer's yeast with a better growing agent. NRRL settled on corn steep liquor. This by-product of corn starch was in plentiful supply, and its potency at promoting mould growth had been recognised and exploited in the US just a few years earlier.

Finally came the quest to find a more productive strain of penicillin. Initially this involved collecting soil samples from wherever in the world the US Army could gather them, and shipping them back to Peoria for the scientists to analyse. This process was cut short when a mouldy cantaloupe found in a market in Peoria itself turned up in the lab. This yielded a mould known as *Penicillium chrysogeum*, which was 200 times more potent than the previous strain. Legend has it the vegetable was found by the lab assistant Mary Hunt, who as consequence earned the unlovely moniker of "Mouldy Mary".

History is made

Taken together these advances pushed the production of penicillin onto a whole new scale. "From having it only in principle they go in a short time to having an actual working mass-production plant," says Robert Bud. "And from the time the Oxford group get involved to the end of the war, we have one of the key breakthroughs in medical history."

In 1943 the US pharmaceutical industry was producing millions of units of the drug a month; by 1945 it was billions. Whereas infection was once a major cause of death among combatants, penicillin had reduced it to a minor threat. Civilian populations began to get the benefits of the new wonder drug from 1945 onwards. The age of the antibiotic was here.

Yet another big step forward came in 1945, with Dorothy Hodgkin using X-ray crystallography to verify the chemical structure of penicillin, paving the way for its eventual synthesis in 1957. Also in 1945, Fleming, Florey and Chain were awarded the Nobel Prize in Physiology or Medicine "for the discovery of penicillin and its curative effect in various infectious diseases". In just 17 years since that September morning, the new wonder drug had changed medicine beyond all recognition, though even then, in his acceptance speech, Fleming warned of the dangers of its misuse... BMS

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Legionella pneumophila	*Influenza A subtype H1N1/2009*
Bordetella pertussis	*Influenza A subtype H1*
	Influenza A subtype H3
	Influenza B
	Coronavirus 229E
	Coronavirus HKU1
	Coronavirus NL63
	Coronavirus OC43
	Parainfluenza virus 1
	Parainfluenza virus 2
	Parainfluenza virus 3
	Parainfluenza virus 4
	Respiratory Syncytial virus A/B
	Human Metapneumovirus A/B
	Adenovirus
	Bocavirus
	Rhinovirus/Enterovirus

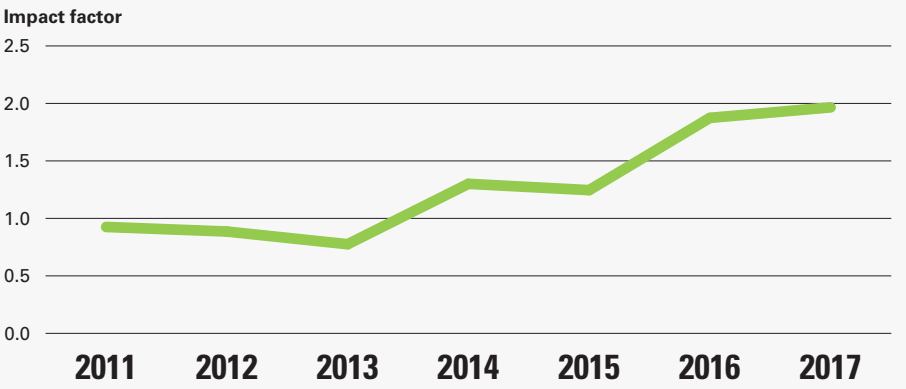
The QIAstat-Dx (DiagCORE) is intended for in vitro diagnostic use in Europe.

Sample to Insight

ON THE RISE

The *British Journal of Biomedical Science* impact factor has increased again, but how is the figure calculated and what does it mean?

SCATTERPLOT OF IMPACT FACTOR VS YEAR



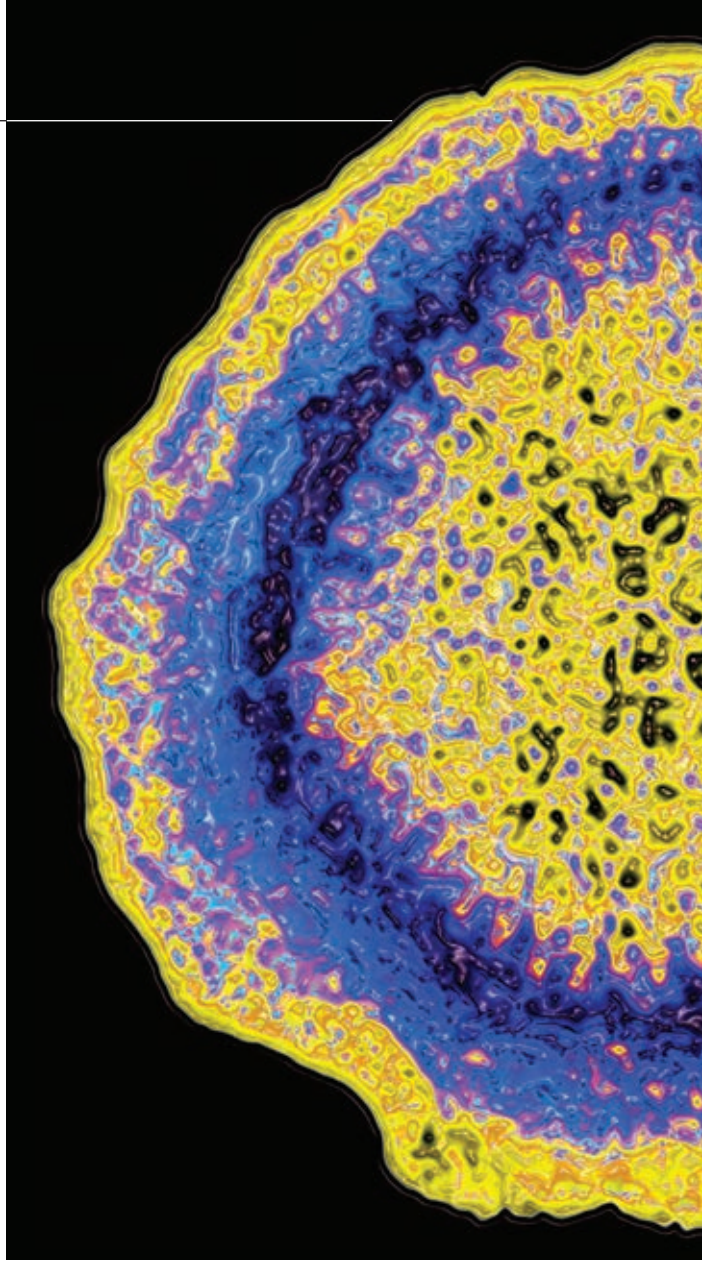
One of the ways in which the quality of a journal can be assessed is its impact factor. This number simply divides the number of citations that a journal has accrued during the last few years (that is, the number of times any paper is cited by a different author in their own paper), and the total number of papers published by that journal in that year. So, if no other researcher ever cites an article in a particular journal, its impact factor will be zero. It follows that papers in very influential journals, such as *The Lancet*, will be cited frequently, and in 2016 *The Lancet*'s impact factor was 47.83 – very large indeed. That of *The British Medical Journal* in 2017 was 23.29, whilst the *Journal of Clinical Pathology*' has a score of 2.89. The organisers of this scheme – the Institute for Scientific Information – also classifies journals in sections, such as cancer and immunology, ours being "Medical Laboratory Technology". Other journals in this section include *Clinical Chemistry* and *Annals of Clinical Biochemistry*, which have impact factors of 8.01 and 1.98, respectively. Other journals carrying data in common with our journal include the *Journal of Clinical Laboratory Analysis*, with an impact factor of 1.303, whilst the *International Journal of Medical Laboratory Research* scores 0.216.

For years, the impact factor of our journal has been around 1.0, sometimes a little above, sometimes a little below. But in the past few years, this has been slowing increasing, and is at present 1.97 (see figure 1, above).

The reason for this is that more of the articles we publish have themselves been cited by other researchers, which in turn means the overall quality of the journal is increasing. Perhaps the primary reason for this is that we moved to submission by website in 2015, enabling the more rapid processing of submissions – a feature highly sought-after by authors. Hopefully, this process will continue. Researchers naturally hope their work will gain wide acceptance, and so will submit to those journals with a good reputation (i.e. a high impact factor, like *the Lancet*). The increase in impact factor will promote a virtuous cycle, as the better the quality of a journal, the more likely is it to receive quality material, which will be cited, leading to an improvement in the impact factor. Indeed, the average number of a group of patients in cohort studies that we have published rose from 90 in 2016, to 126 in 2017 and to 147 so far this year. Similarly, numbers of subjects in case/control studies was 106/75 in 2016, 174/65 in 2017, and is 199/140 so far this year. Increased numbers (formally described as power) naturally brings increased confidence that the results are likely to be correct, and so increased likelihood of the work being cited.

Whether this trend will continue cannot be predicted, but it is good to know that our journal, and so our vocation, is on the rise. BMS

Andrew Blann, is the Editor of the *British Journal of Biomedical Science*



British Journal of Biomedical Science Issue 4 2018: a synopsis

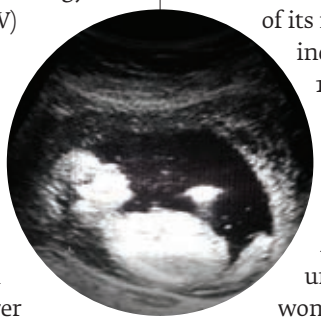
The hard copy of the autumn issue of our journal is complete. Editor **Andrew Blann** outlines the content of the latest issue, which includes six papers that use techniques in molecular genetics.

LIVER DISEASE

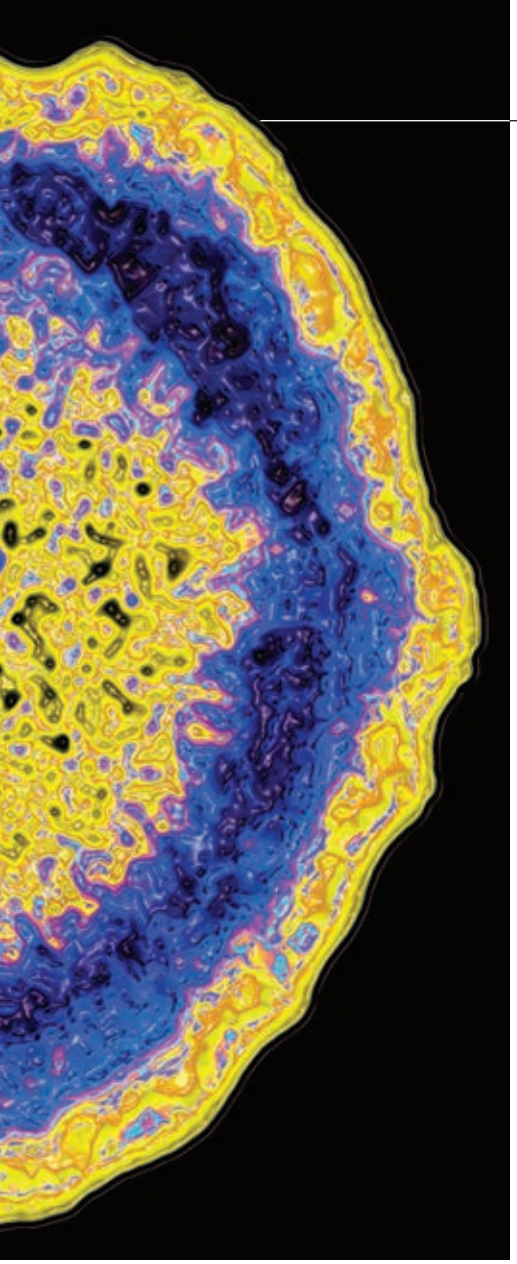
Hepatitis C virus infection is a major problem in many parts of the world and in many cases leads to hepatocellular carcinoma (HCC). Attallah and colleagues (pages 157-162) studied 500 subjects infected with the virus, reporting that those with certain SNPs in *IL28B* are at risk of developing liver fibrosis, cirrhosis and HCC, suggesting that knowledge of these genotypes may help diagnosis and target treatment. El-Bendary *et al.* (pages 175-181) also looked at SNPs in chronic hepatitis C virus infection, finding that certain alleles in genes for Toll-like receptors (TLRs) 3, 4 and 7 seem to confer protection from, or predispose to, chronic infection with the virus.

The MELD score, derived from bilirubin, INR and creatinine, aims to quantify the severity of liver disease. Elalfy and colleagues (pages 187-191) hypothesised that any one of a series of full blood count indices, and their combinations, could predict the recurrence of hepatocellular carcinoma after a form of treatment – transarterial chemoembolization. They found that the granulocyte/monocyte to lymphocyte ratio is comparable to the MELD score in predicting recurrence – interesting news for the haematology lab!

Chronic hepatitis B virus (HBV) infection often leads to cirrhosis and carcinoma, but the process is unclear. Mousa and colleagues (pages 192-196) hypothesised links between serum leptin and the homeostasis model of insulin resistance (HOMA-IR), and liver fibrosis in a group with chronic HBV infection. Unlike routine LFTs (all of which were of course, abnormal), both HOMA-IR and leptin were significant independent predictors of HBV infection, and leptin correlated very strongly with the degree of fibrosis, point to value as a diagnostic and staging marker.



Non-alcoholic fatty liver disease (NAFLD) is a common form of chronic liver disease worldwide, but knowledge of its impact into pregnancy is incomplete. Mousa *et al* (pages 197-199) found that pregant women with NAFLD were more likely to have gestational diabetes, pre-eclampsia, and raised AST, total cholesterol and uric acid than pregnant women free of NAFLD.



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GASTRIC AND CERVICAL CANCER

Although gastric cancer is a common malignancy, there are no reliable blood markers.

Zhao *et al* (pages 203-205) tested the hypothesis of a link between serum soluble major histocompatibility complex class I-related chain A (sMICA) and clinicopathological features in gastric cancer, finding levels to be higher in the disease, and that such levels were linked to metastases and 5-year survival outcome. Could sMICA be the first blood test in this disease?

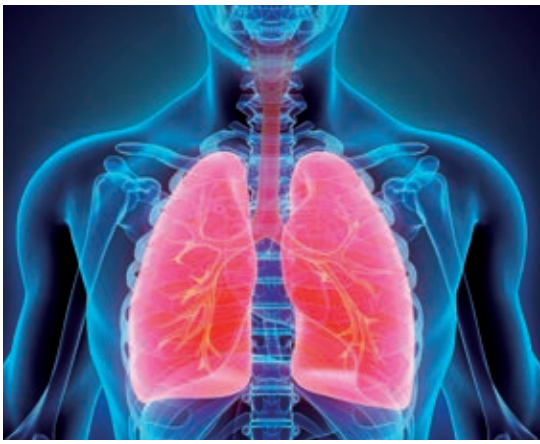
A common problem with the chemo- and radiotherapy of cervical is toxicity towards certain organs and tissues, believed to be due to reactive oxygen species (ROS). Abbas *et al* (pages 169-174) report that certain SNPs in the gene for an antioxidant enzyme, glutathione S-transferase, theoretically protective of these metabolic toxins, are linked to the likelihood of severe gastrointestinal toxicity, once more pointing to value in diagnosis and management. MicroRNAs (miRNAs) are small ribonucleic acid heteropolymers, *STAT3* is a signal transduction factor that passes activation messages to the nucleus: both are linked to malignancy. Mirnoori and colleagues (pages 182-186) hypothesised alterations in pri-miR-124-1 and STAT3 in 250 gastric cancer patients and 310 controls, finding that certain SNPs are indeed linked to the disease.

"Few of use can be unaware of the growing problem of microbial resistance to antibiotics"

MICROBIOLOGY, DIABETES AND IMMUNOLOGY

Although the leading aetiology of diabetes is obesity and hypergylcaemia, these do not account for all disease as several genes are implicated. In a study of 250 diabetics, Abbas and colleagues (pages 163-168) also looked for SNPs in the gene for TLR4, and found links with three common co-morbidities – hypertension, nephropathy and/or dyslipidemia - again suggesting the analysis of these SNPs may help diagnosis and management. Since cell-surface TLRs are part of the innate immune system, recgonthis report supports the hypothesis of inflammation and diabetes.

Few of use can be unaware of the growing problem of microbial resistance to antibiotics, and extended spectrum beta lactamase [ESBL] producers and ESBL associated cephalosporin resistance among *Acinetobacter baumannii* is emerging. Smiline and colleagues (pages 200-202) analysed the distribution of certain plasmid encoded beta-lactamase genetic determinants likely to be linked to



resistance, in 73 isolates. They found *blaTEM* and *blaSHV* in 57.5% and 6.8% respectively, but none of the strains showed the presence of *blaCTX-M*, pointing the way to those seeking a panel of genes in this setting.

Bactericidal/permeability-increasing protein (BPI) is one of the antigens recognised by anti-neutrophil cytoplasmic antibodies (ANCA). Tian and colleagues (pages 206-208) hypothesised a role for these antibodies in chronic obstructive pulmonary disease (COPD). Lung function tests were worse in BPI-ANCA(+) patients, who also had longer disease duration and history of hospitalisation. In 12 and 18 months of follow-up, all clinical indices had deteriorated more in the presence of the antibodies, a finding that be used to help drive treatment and subsequent monitoring. BMS

Andrew Blann is the Editor of the *British Journal of Biomedical Science*

One or more of these articles may be the subject of a Journal-based learning exercise for those seeking to improve their continuing professional development profile.

HOW TO... ENSURE CORRECT CALIBRATION

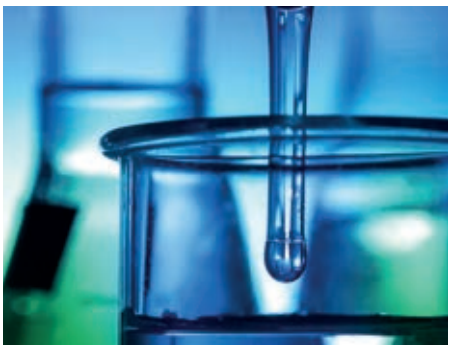
Specialist Biomedical Scientist **Dan Kelly** looks into linear calibration curves, Beer-Lambert's law and IQC interpretation.

In the clinical biochemistry laboratory, it is important to appreciate and understand the fundamental principles of calibration curves and how to interpret results, as the quality of these determine whether IQC values pass or fail internal rules set by the laboratory.

Two-point linear calibration curves are the most commonly used type of calibration for spectrophotometric methods in the biochemistry laboratory. These calibrations typically use a blank and a known concentration of high standard to construct a straight calibration curve that is subsequently used to calculate the unknown concentration of samples. These linear curves are mathematically determined by Beer-Lambert's law, this law describes the relationship between the absorbance (A), and three independent variables: molar absorptivity (e), path-length (l), and concentration (c). The law takes the form of y=mx+b, where m is the slope or gradient, b is the y intercept, y is the absorbance and x is the concentration. Thus, Beer-Lambert's law describes the linear relationship between absorbance and concentration of an absorbing species, and is mathematically written as: A=exlxc.

The relationship between a calibration curve and IQC values are fundamentally important in clinical biochemistry. Deviations in the calibration curve can significantly affect IQC values observed by the laboratory, it is here where skilled interpretation and understanding is needed. When a poor calibration has been performed the calibration correction factor (CF) values change causing significant changes in the calculation of unknown samples. The CF value is the number added to the initial value so a true value is calculated. As such, during analysis the absorbance of an unknown sample is multiplied with the factor for result calculation.

Significant calibration changes cause substantial shifting of IQC values that



span the linearity of the assay, and are associated with positive or negative shifting when observed on the Levey-Jennings plot, depending on how the curve has drifted. However, when subtle calibration changes occur and the trajectory of the curve has changed, this is where interpretation of IQC errors is fundamentally important in analytical chemistry. An example of such calibration change is highlighted in figure 1. The calibration highlighted in Red is a passed calibration curve for an assay that conforms to the standard values provided by the manufacturer. This curve has the correct trajectory that can accurately calculate the concentration of the unknown using Beer-Lambert's law. The concentration of the IQC is 0.4 that should produce absorbance values of 1.0, arbitrary values.

Conversely, the calibration curve in blue is an example of an incorrect

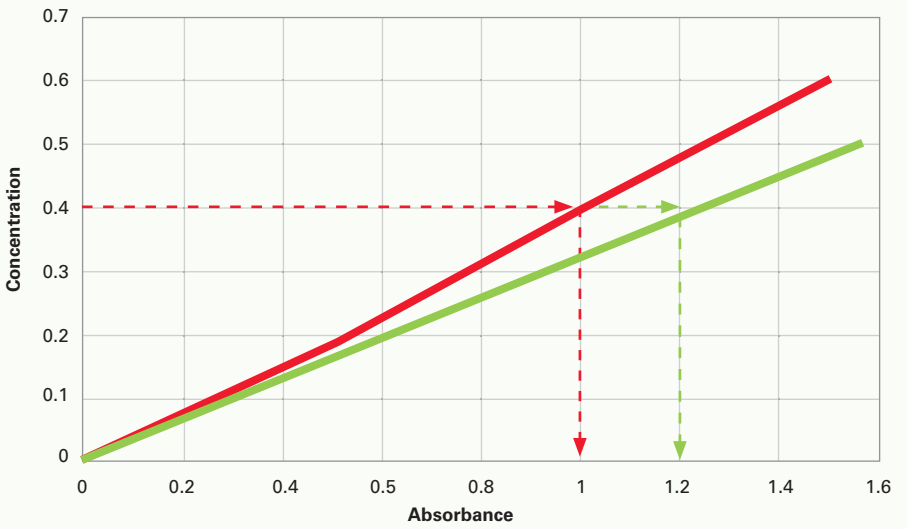
IMAGES: ISTOCK

calibration, this curve is spanning the linearity of the assay at a lower gradient, which will cause a deviation in the calculation of the unknown. The CF values have shifted significantly when compared to previous values; which has caused an upward shift in the IQC data. Subsequently, the same IQC material will produce absorbance results of 1.2. As displayed, the same material can produce different results when the calibration curve has shifted slightly. This example can be applied for calibration curves that have shifted at a steeper gradient, which will produce IQC results that are lower than set target ranges.

Calibration shifting mentioned in the example may be due to a number of factors that influence assay performance, such frequent examples include: incorrect reconstitution of calibration standard material, old calibrator material that has deteriorated, contamination, inherent analytical issues, reagent performance issues. As an analytical chemist, it is important to note that excessive calibration frequency causes erratic IQC values and this practice should be avoided. It is important, therefore, to review calibration curves appropriately when investigating IQC shifts. Reviewing and interpretation of data should be commonly employed in the clinical chemistry laboratory to ensure patient results are being reported accurately. Significant changes in calibration curves cause substantial changes to IQC values that are easily recognised. However, when subtle shifts in calibration data slightly alter the trajectory of the curve there is a modest shift in IQC data. It is here where a review of CF values and calibration history may be needed to determine the cause of a QC failure. BMS

Significant calibration changes cause substantial shifting of IQC values

CALIBRATION CURVE AND IQC SHIFT



Dan Kelly is a Specialist Biomedical Scientist, working in clinical biochemistry at Leeds General Infirmary.

MY IBMS NEWS

PROMOTE THE SECTOR

NATIONAL PATHOLOGY WEEK

The IBMS is encouraging member's to get involved in National Pathology Week, which takes place next month.

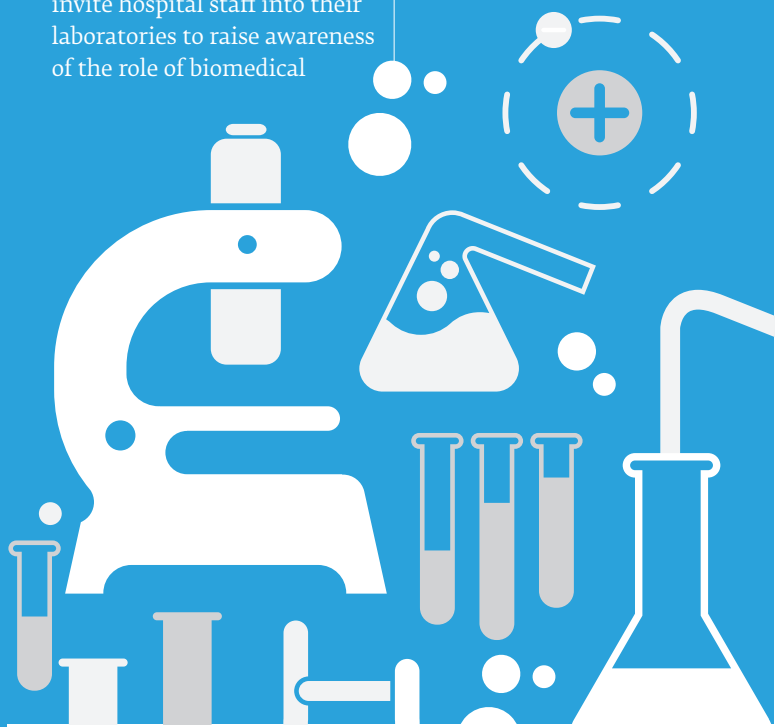
It is the Royal College of Pathologists' annual celebration of the sector and highlights the vital role that biomedical scientists and support staff play in the diagnosis of disease and the provision of healthcare.

The week will run from 5 to 11 November and the IBMS is encouraging members to invite hospital staff into their laboratories to raise awareness of the role of biomedical science in healthcare.

The IBMS provides packs of free promotional items all year round for any events or stands that aim to inform or promote biomedical science.

Any members wanting materials in time for National Pathology Week will need to submit their request before 26 October.

→ Members interested in promotional materials should visit the resources section of the IBMS website.



RESEARCH

IBMS commissions membership survey

The IBMS has commissioned Research by Design to undertake a project to understand more about members' relationship with the Institute.

The research will give the IBMS a clearer understanding of the requirements and views of IBMS members, specifically what members value from their membership, their expectations of the Institute and their future aspirations for the IBMS.

The consultation process has already involved in-depth interviews with a number of members, and is now being followed by an online quantitative survey involving all members.

The online survey will be live during October and all members are encouraged to share their views.

→ Any members who have additional questions, or would like further information about the project, are asked to contact Lizzie Simkin at Research by Design on lizzies@researchbydesign.co.uk.

→ Alternatively, for queries relating more specifically to the IBMS, please contact Lynda Rigby on LyndaRigby@ibms.org

IBMS GROUP

SCOTLAND QUALITY MANAGEMENT

The IBMS Scottish Quality Management Discussion Group will hold the autumn meeting in the Teacher Building in Glasgow on 16 November.

Those interested or working in quality management are encouraged to register with Eventbrite to attend, with discounted registration for IBMS members.

Speeches will cover change management, GDPR, duty of candour, verification and validation. There will also be with an opportunity for Q&A and a quality quiz with prizes.

It is a chance to discuss quality management challenges, share good practice and is a good CPD opportunity.

For those who wish to attend, a pre-meeting dinner is arranged for 15 November.

OBITUARY

EVE WOODBRIDGE FIBMS (AGED 84)

Eve always wanted to study biomedical science. However, her Irish Catholic background posed problems in Dublin as she wished to study at a Protestant institution. Undaunted, Eve eventually received special permission from Dublin's bishop to study at Trinity College. She then joined the National Blood Transfusion Centre in Dublin as a student technician at 18.

Eve's success in the profession raised eyebrows during the post-war period. *The Irish Times* received complaints because a woman had taken what was then seen as a man's job. Undeterred, Eve continued to work within the profession, later joining the team at the Mater Misericordiae Hospital in Dublin, where she worked in haematology and bacteriology.

Eve relocated to the UK to work at the Royal Free Hospital in Islington, specialising in cytology. She then got married and had two children while running a successful pub with her husband. When the family relocated to Essex, she joined St Andrew's Hospital cytology department, where she worked until retirement, having become Head of Department.

In 1952, Eve joined the IBMS, became an IBMS Fellow 10 years later and in 2002 was awarded the IBMS's prestigious 50 Year Medal, for continuous membership with the Institute.

Eve is fondly remembered by her children, who credit her determination and refusal to give up, as contributing hugely to their successes in life. They said: "Even 20 years after she retired, she still kept up to date with the profession, reading the monthly *Biomedical Scientist* magazine. She remained sharp as a tack and was a remarkable woman."

PRESIDENT'S PRIZES
Continuing the coverage of winners from around the country

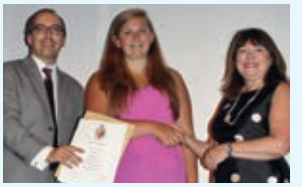
PRESIDENT'S PRIZE WINNERS

These prizes are awarded to students graduating from IBMS-accredited BSc Hons programmes who have achieved academic distinction

UNIVERSITY OF SURREY

Pippa Durrant was awarded the IBMS President's Prize at the University of Surrey. Her placement year was completed at St George's University of London, where she undertook the role of a Clinical Research Assistant and in her dissertation investigated the presence of a potentially novel B lymphocyte subpopulation in older people. Pippa hopes to complete the IBMS Registration Training Portfolio to become a biomedical scientist.

UNIVERSITY OF BRIGHTON



Sophie Paterson was awarded the IBMS President's Prize at the University of Brighton where she graduated with a BSc (Hons) Biomedical Science sandwich degree. Sophie completed her placement at Brighton and Sussex University Hospital at the Crawley site in the haematology laboratory, where she has subsequently been employed. She is pictured here with Professor David Timson, Head of School (Pharmacy and Biomolecular Sciences) and Joyce Overfield, IBMS National Council Member.

KINGSTON UNIVERSITY

Nancy Aguoru received an IBMS President's Prize at a Kingston University ceremony held earlier this year. Following her degree course success, she secured a position in a London hospital where she will complete an IBMS Registration Training Portfolio, while in the longer term she aspires to complete a PhD in biomedical science. Pictured are Paul Waller, Sue Alexander, Nancy Aguoru and Course Director Dr Steve Robinson.

UNIVERSITY OF BRADFORD

Cassie Harold was the recipient of this year's IBMS President's Prize presented at the University of Bradford. Cassie, pictured receiving her award from Zeshaan Ejaz committee member on both the IBMS West Riding branch and IBMS Yorkshire Region Branch, has started a Masters in Experimental Medicine course at Queen's University, during which she will utilise the skills and qualities developed while studying at Bradford.

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DEADLINE WEDNESDAY 2 JANUARY 2019

Genetic polymorphisms in *KCNJ11* (*E23K, rs5219*) and *SDF-1*β (*G801A, rs1801157*) genes are associated with the risk of type 2 diabetes mellitus.

Rizvi S, Raza ST, Mahdi F, Singh SP, Rajput M, Rahman Q. *Br J Biomed Sci* 2018; **75** (3): 139–44. Assessment No G101018

01	More than 150 distinct genetic loci, with more than 120 variants, have been identified that may be involved in the pathogenesis of diabetes.
02	Type 2 diabetes has a multifactorial aetiology, where genetic factors in combination with environmental factors confer risk of disease development and progression.
03	Genetic alterations in *KATP* are associated with diabetes due to the effect of KCNJ11 channels on insulin secretion.
04	Genomic DNA was extracted from peripheral blood leucocytes using the standard phenol-chloroform extraction method.
05	Fasting blood sugar was measured by the glycerol phosphate oxidase–peroxidase amidopyrine method.
06	Cases and controls were matched for age (45 and 46 years, respectively) and gender (99 males/101 females and 98 males/102 females, respectively).
07	Mean creatinine level was 70 µmol/L in healthy controls and 50 µmol/L in cases.
08	Polymorphisms in *KCNJ11* result in neonatal diabetes and congenital hypo-insulinaemia.
09	Studies have shown that the *rs5219* variant may alter the charge of the ATP-binding region and decrease channel sensitivity to ATP.
10	Stromal cell derived factor-1 (SDF-1), also known as CXCL12, is a peptide chemokine that is coded for by a gene on chromosome 10q11.1.
11	Many of the published links between polymorphisms in *KCNJ11* and *SDF-1β* and diabetes consider multiple genotype models.
12	Figure 1 shows a 3% agarose gel picture of *MspI*-digested products.
13	A number of risk alleles for diabetes and mutations in several genes may add up and predispose an individual to increased risk of disease.
14	Distribution of *SDF-1β* (*G801A, rs1801157*) genotypes according to dominant, recessive and additive models showed no significant differences in dominant and additive models between cases and controls.
15	Genetic factors are now regarded as the leading cause of diabetes.
16	ATP-sensitive potassium channels (KATP) are transmembrane proteins present on beta cells.
17	Genotyping data were compared between cases and controls using the $\chi 2$ test.
18	In this study, genetic polymorphism analysis was performed by loop-mediated isothermal amplification.
19	*G801A* polymorphism has been studied in various diseases, including diabetes, HIV infection and cancer.
20	In this study, the frequency of AA genotype in cases was 4.5%, which was lower than reported in Iranian diabetics.

Potential value of circulating microRNA-126 and microRNA-210 as biomarkers for type 2 diabetes with coronary artery disease.

Amr KS, Abdelmawgoud H, Ali ZY, Shehata S, Raslan HM. *Br J Biomed Sci* 2018; **75** (2): 82–7. Assessment No C101018

01	The International Diabetes Federation (IDF) listed Egypt among the world's top 10 countries in the number of patients with diabetes.
02	MicroRNAs are highly conserved large non-coding endogenous RNA molecules involved in the regulation of key processes such as proliferation, differentiation, apoptosis and metabolism.
03	MiR-210 is abundantly expressed in endothelial cells, maintains endothelial homeostasis and vascular integrity via regulating several components of the vascular endothelial growth factor pathway.
04	Plasma miRNAs are potential non-invasive biomarkers for the diagnosis and prognosis of many diseases.
05	miR-126 levels are reduced in diabetes, while miR-210 levels are raised in diabetes.
06	Type 2 diabetes is a metabolic disorder characterised by insulin resistance and pancreatic α-cell dysfunction.
07	In this study, venous blood samples for glucose determination were taken into K-EDTA tubes.
08	Plasma relative expressions of miR-126 and miR-210 were 0.38 ± 0.03 and 5.3 ± 0.56 in diabetes alone versus 0.08 ± 0.03 and 21.44 ± 0.97 in diabetes with coronary artery disease (CAD).
09	Quantitative real-time polymerase chain reaction (qRT-PCR) was performed using a TaqMan microRNA assay for 40 cycles in duplicate reactions containing the prepared cDNA.
10	Area under the curve (AUC) for plasma miR-210 in type 2 diabetic patients with CAD versus controls was 0.95.
11	High-density lipoprotein cholesterol (HDL-c) level (mean ± SD) in the control group was 1.0 + 0.6 mmol/L.
12	A total of 100 patients with type 2 diabetes and 100 controls were enrolled in the study.
13	The results showed no significant difference in age and gender between the three groups studied.
14	In patients with diabetes alone there was a significant inverse correlation between miR-126 and fasting glucose and HbA1c.
15	There was a significant difference in disease duration between the diabetes group and the diabetes with CAD group (P<0.001).
16	The ROC curve of miR-210 significantly discriminated between both patient groups and controls as well as between diabetes patients with and without CAD.
17	Low serum levels of miR-210 have been reported in rheumatoid arthritis.
18	The epigenetic effect of miR-126 is encoded within an intron of Egfl7.
19	miR-210 promotes vascular endothelial growth factor (VEGF) signalling by suppressing two negative regulators of the VEGF pathway.
20	Ordinal logistic regression analysis revealed a significant association between groups and miR-126 and HDL-c.

REFLECTIVE LEARNING

01	Type 2 diabetes mellitus (T2DM) is a global health problem resulting from the interaction of environmental and genetic factors. Based on the results of a literature search, what other genetic factors have been implicated in T2DM?	01	Micro-ribonucleic acids (miRNAs) are currently in the spotlight as post-transcriptional regulators of gene expression, and the field of miRNAs in cardiovascular biology and disease has expanded at an incredible pace. Discuss the implications for pathology.
02	Explain the difference between the terms dominant, recessive and additive in relation to the effects of different genotype models.	02	MicroRNAs in diabetes and diabetes-associated complications. Discuss.

A wide range of training courses, CPD and local events and activities is listed below. Members are advised to contact organisers for further information. A full list is available on the IBMS website.

EVENTS AND TRAINING COURSES

DATE	TITLE	VENUE CONTACT
October		
1-26 Oct	**Introductory course in gynaecological cytology**	Harrow I LNWH-tr.lrctcbooking@nhs.net
4 Oct	**UK NEQAS reproductive science semen analysis one-day workshop**	Manchester I repscience@ukneqas.org.uk
4 Oct	**ISO accreditation for POCT**	Leicester I nichola.cadwallader@sbk-healthcare.co.uk
8-12 Oct	**Introduction to the principles and practices of working safely at ACDP containment Level 3**	Porton Down I nadp.training@phe.gov.uk
9 Oct	**HPLC troubleshooting**	Reading, Scotland, Manchester I jsumner@hichrom.com
9 Oct	**Intermediate immunohistochemistry**	Sheffield I l.baxter@sheffield.ac.uk
10 Oct	**BSAC antimicrobial susceptibility testing user day**	Birmingham I ecarruthers@bsac.org.uk
10 Oct	**HPLC method development**	Reading, York, Scotland, London, Manchester I jsumner@hichrom.com
11 Oct	**Quality, audit and improvement workshop**	Croydon I sue.alexander@rmh.nhs.uk
13 Oct	**Biomed online learning courses**	London I c.e.ronan@gre.ac.uk
17 Oct	**One-day update in cervical cytology audit**	Bristol I SWRCTC@nbt.nhs.uk
17 Oct	**UK NEQAS Cellular Pathology Technique tissue morphology and recognition workshop**	Gateshead I chantell.hodgson@nhs.net
18 Oct	**Management and leadership essentials workshop**	Croydon I sue.alexander@rmh.nhs.uk
18 Oct	**UK NEQAS Cellular Pathology Technique tissue preparation techniques workshop**	Gateshead I chantell.hodgson@nhs.net
19 Oct	**Back to the future IV inborn errors of metabolism**	Manchester I june.Petty@mft.nhs.uk
19 Oct	**Educational workshops 2018: the ongoing challenges of MRSA**	Cardiff I ecarruthers@bsac.org.uk
19 Oct	**Going overboard with microbiology – "women and children first"**	Liverpool I swallis@mastgrp.com
22 Oct	**Update course in gynaecological cytology – HPV update and glandular lesions**	Birmingham I amanda.lugg@bwnft.nhs.uk
26-28 Oct	**Midland CELLibration**	Daventry I karen.mcleod2@nhs.net
30 Oct	**Educational workshops 2018: the ongoing challenges of MRSA**	Newcastle I ecarruthers@bsac.org.uk
November		
5 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Birmingham I ecarruthers@bsac.org.uk
6 Nov	**Advancing management skills workshop**	Croydon I sue.alexander@rmh.nhs.uk
6 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Salisbury I ecarruthers@bsac.org.uk
7 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Dublin I ecarruthers@bsac.org.uk

MEETING MICROBIOLOGY LABORATORY DEMANDS THROUGH AUTOMATION

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HERE TO HELP

FIRST DAY PLACEMENT NERVES

Sometimes the first few weeks might be overwhelming for trainees, but they should be considered an investment in the future, writes **Jocelyn Pryce**, Head of Registration and Training at the IBMS.

The work of the Education Team is not driven by either the seasonal or academic calendar but, as summer draws to a close, our thoughts turn to the thousands of students who are beginning their new academic year, especially those joining laboratories as placement students from our accredited universities and the training teams supporting them. Although not all begin their placement at the start of the academic year, a large proportion do and this influx of inexperienced trainees can place a strain on those delivering the training.

Many training teams have strong, well-coordinated training programmes in place, which provide framework support for both the laboratory staff and the trainees and such good organisation can go a long way to ensuring a successful outcome for the student at the end of the placement period. Preparation for the arrival of new trainees should trigger reflective thought in those of us who have been through this cycle before: Do we remember what it was like on our first day? Do we have a mentor who we look back on and thank for introducing us to this interesting career? Do we remember how it felt to learn about biomedical science for the first time, or were we just born experts? Of course we weren't; we've all had first day nerves wondering what would greet us and whether we would love the career we were stepping into.

Thinking outside of the induction process to the wider introduction you give your trainees in their early days can make the process much more comfortable for them. We expect them to have been prepared in the practical sense in terms of what they can expect, but are they prepared mentally for what they are about to undertake? Sometimes the first few weeks can be overwhelming and progress may feel slow. Trainees can feel that they are failing to progress at the speed they expect and trainers may be frustrated by the reliance a trainee has on them. Consider trainees as an investment of your time in the next generation, one day you may be the scientist that they reflect on as the mentor who introduced them to biomedical science.

Placement models are dependent on the ability of employers to provide them. A flexible approach has been taken to this aspect of degree accreditation and, as long as our standards are met, some placements may be shorter than the recommended year-long approach to the registration portfolio. These were agreed on the basis that elements of the portfolio are covered in the academic curriculum and that the placement period is an intensive, accelerated training period provided jointly by the university and training team in the laboratory. This brings me nicely on to our myth-busting for this month. The registration portfolio should be an artefact of that period of training containing evidence that demonstrates an immersion in laboratory life and atmosphere, not a workbook where a trainee approaches it as a series of tasks to be undertaken. If it is approached in this way, the trainee loses a great deal of the experience that was so important in our own development. So, when reflecting, think carefully about being immersed in the atmosphere of the laboratory and try to provide your trainees with that experience too.

As trainers, your ability to reflect and put yourself back in their shoes might make all the difference.

IMAGE: ISTOCK

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Blood Transfusion Quality Manager

Band 8a based in Chelsea, London (working cross site Chelsea & Sutton)

Permanent, Full-Time 37.5 hours per week

Job ref: 282-SA5427-B

Salary Band 8a £49,077 £56,632 pa inc

This is a newly established post offering a unique opportunity for an enthusiastic and knowledgeable individual to enhance our Blood Transfusion Quality Management System compliant with the requirements of the Blood Safety & Quality Regulations.

Blood Transfusion Section Leader

Band 7 Chelsea site

Permanent, Full-Time 37.5 hours per week

Job ref: 282-SA5361-B

Salary Band 7 £39,866 - £49,704 pa inc

Working with the BT Quality Manager you will be responsible for the day to day functioning of this section within Blood Sciences. You should be able to work across teams, in a busy environment handling complex surgical cases.

The Trust offers study leave support, in house personal development courses and the opportunity to work flexibly. There is free Trust transport between sites and between Sutton Station and the RM Sutton site.

To apply and/or further details please visit: http://jobs.royalmarsden.nhs.uk/job/ and search by reference number
Closing date: 21 October 2018.

The Trust reserves the right to amend the closing date of job vacancies at any time.

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NHS

UK NEQAS CELLULAR PATHOLOGY TECHNIQUE QUALITY MANAGER

(AfC band 7) 1.0 – PERMANENT CONTRACT

SALARY: £33,222 - £43,041 PER ANNUM (FULL TIME – 37.5 HOURS PER WEEK)

NHS JOBS REF: 297-1819-1261

An exciting job opportunity has arisen within UK NEQAS CPT for a Quality Manager. UK NEQAS Cellular Pathology Technique (CPT) is an international organisation providing a comprehensive range of accredited EQA and proficiency testing programmes for all aspects of tissue diagnostics.

The post holder will be responsible for the design, implementation, monitoring and management of the Quality Management System (QMS), ensuring compliance to ISO/IEC 17043:2010(E). They will extract, manipulate and statistically analyse data produced by UK NEQAS CPT, in order to provide information and feedback to participants and users, in the form of audits, reports, surveys and KPI's.

The successful candidate will have excellent interpersonal, communication and organisational skills, and act as deputy to the Scheme Manager, to communicate effectively with staff, participants and users.

Applications are invited from enthusiastic, innovative and forward thinking candidates who are able to prioritise their own workload, work as part of a team, and adapt quickly and efficiently. Previous involvement with audit, EQA, IQC and quality management to ISO standards is essential.

Health Care Professions Council Registration and attained Masters Degree / Higher Specialist Portfolio / IBMS Fellowship, or equivalent experience and knowledge, is essential to enable the post-holder to provide expert advice to users of the service. Personal development towards a qualification in Quality Management will be supported. Knowledge, experience and competency in specialised diagnostic cellular pathology techniques is desirable.

Informal enquiries welcomed by Mrs Chantell Hodgson via e-mail: chantell.hodgson@nhs.net or by telephone on (0191) 445 5566.

UK NEQAS
Cellular Pathology Technique

NHS
Manchester University
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AIMING HIGHER

RECRUITMENT OPEN DAY 9 OCTOBER 2018 - 3pm to 7pm
The Nowgen Centre, Manchester

OPPORTUNITIES AVAILABLE:

Band 8d Head of Service Laboratory Haematology
Band 8b Laboratory Manager for the Greater Manchester Immunology Service
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Band 8a Lead BMS Biochemistry
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Biomedical Scientist – Microbiology (Ref: IRC17421)

NHS Shetland

An opportunity to work with the Island Medics

Full Time Band 6 role - Salary Range Band 6: £27,635 - £37,010 per annum plus Distant Island Allowance of £1,738 per annum. Excellent relocation package of up to £8,000

NHS Shetland has an opportunity for a Biomedical Scientist with Microbiology expertise to join the team in the Laboratory, a purpose built facility in the Gilbert Bain Hospital, Lerwick. Serving a population of circa 24k and processing circa 100k samples per annum. The laboratory has close working partnerships with Grampian University Healthcare Trust in Aberdeen and NHS Orkney.

Working as part of a multi-disciplinary clinical diagnostic team offering a service to our small, remote and rural 63 bedded hospital and 10 health centres, you will act in a dual capacity of mainly working in Microbiology (backing up the Band 7 post) but also covering areas in Blood Science. Training will be provided if you do not possess the blood science skills already.

Registered as a Biomedical Scientist with the HCPC, you will have an honours degree or equivalent experience suitable for registration with the Institute of Biomedical Science. Once trained, you will be required to participate in the multi-disciplinary out of hours roster, including lone working at weekends.

Take a sea change and enjoy the opportunity - Shetland is a wonderful place to live and work. Shetland offers low pollution, low crime, excellent schools, great leisure facilities, unique wildlife and amazing scenery, whilst still only a short flight away from the UK mainland. To find out more about living and working in Shetland go to **www.shetland.org**

For further information on the post please contact Robert Wardrop, Laboratory Manager on **01595 743041** or **rwardrop@nhs.net**

Closing date: 28th October 2018

Interviews will be held in Shetland: week commencing 12th November 2018

For more information and to apply:

Internal Applicants: If you are currently working for NHS Shetland (including Bank Members) you must apply via the e:ESS website link: **https://www.jobs.nhsscotland.com/OA_HTML/AppsLocalLogin.jsp**

For details of your e:ESS login for the above link please contact Laura Pottinger on **01595 743031** or email **shet-hb.eesshelpdesk@nhs.net**

External Applicants: i.e. if you are NOT currently an NHS Shetland employee or registered on our Bank, you must apply via the following e:ESS website link:-

https://www.jobs.nhsscotland.com

If you require assistance or encounter any technical issues with your application, please e-mail support at **nss.eess@nhs.net** including the vacancy reference number and "NHS Shetland" in the subject line.

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MY LAB

RED CELL IMMUNOHAEMATOLOGY

Kate Griffiths gives a guided tour of her lab at the headquarters of the Welsh Blood Service.

Nestled in the hilly Welsh countryside, 10 miles north of Cardiff, lies the headquarters of the Welsh Blood Service (WBS). Within the WBS sits the ISO accredited red cell immunohaematology (RCI) laboratory the specialist reference centre for transfusion laboratories in Wales. The RCI team tests approximately 3,500 complex referrals of hospital patient, antenatal and donor samples annually.

The head of RCI laboratory works closely with section leaders in patient and donor referrals, immunohaematology and reagent production to ensure smooth running and high-quality service is provided 24/7.

The department consists of an additional eight qualified biomedical scientists, who are required to participate in an out-of-hours rota, alongside two medical laboratory assistants offering vital daily support. As a very small team, there is great camaraderie and excellent personal relationships.

The team is responsible for complex antibody testing of hospital patient, donor and antenatal referrals, often including compatibility testing. The laboratory has seen gradual increase in referrals, including the impact of patients on monoclonal antibody drug therapy – antibody identification and compatibility testing is impossible with current automated technology. In these situations, manual serological testing is the only solution to finding safe blood for transfusion.

Samples are received throughout the day and are prioritised accordingly.

The immunohaematology section consists of two members of staff responsible for anti-D and anti-c quantitation referrals, fetomaternal haemorrhage estimation by flow cytometry and chemiluminescence test assays.

The department has a reagent production section, responsible for preparing antisera and red cells used in-house. The Welsh Assessment of Serological Proficiency Scheme (WASPS), a UK-wide ISO accredited EQA scheme, is prepared and dispatched by staff in the department. The WASPS scheme was first developed at WBS in 1989 – next year we will celebrate our 30th birthday. Originally aimed at hospitals within Wales, the exercise has expanded, with 75 transfusion laboratories in UK participating in the last exercise.

As a qualified IBMS training laboratory, the staff are involved in a huge array of training, not just for WBS staff, but for staff from hospital transfusion laboratories across Wales. Staff enjoy sharing their expertise in specialist serological techniques and the scientific knowledge behind them.

The laboratory is a placement centre for students completing their Practitioner Training Portfolio and we work very closely with Cardiff Metropolitan University to facilitate this training.

All staff are passionate about biomedical sciences and we were thrilled to win "Video of the Year 2018" in the recent IBMS Biomedical Science Day 2018 Awards. The WBS gives us the opportunity to develop ourselves and others while maintaining an excellent standard of care for our patients and customers.

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