ONE-TO-ONE

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FIFTY YEARS OF NEQAS

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WAR ON CANCER

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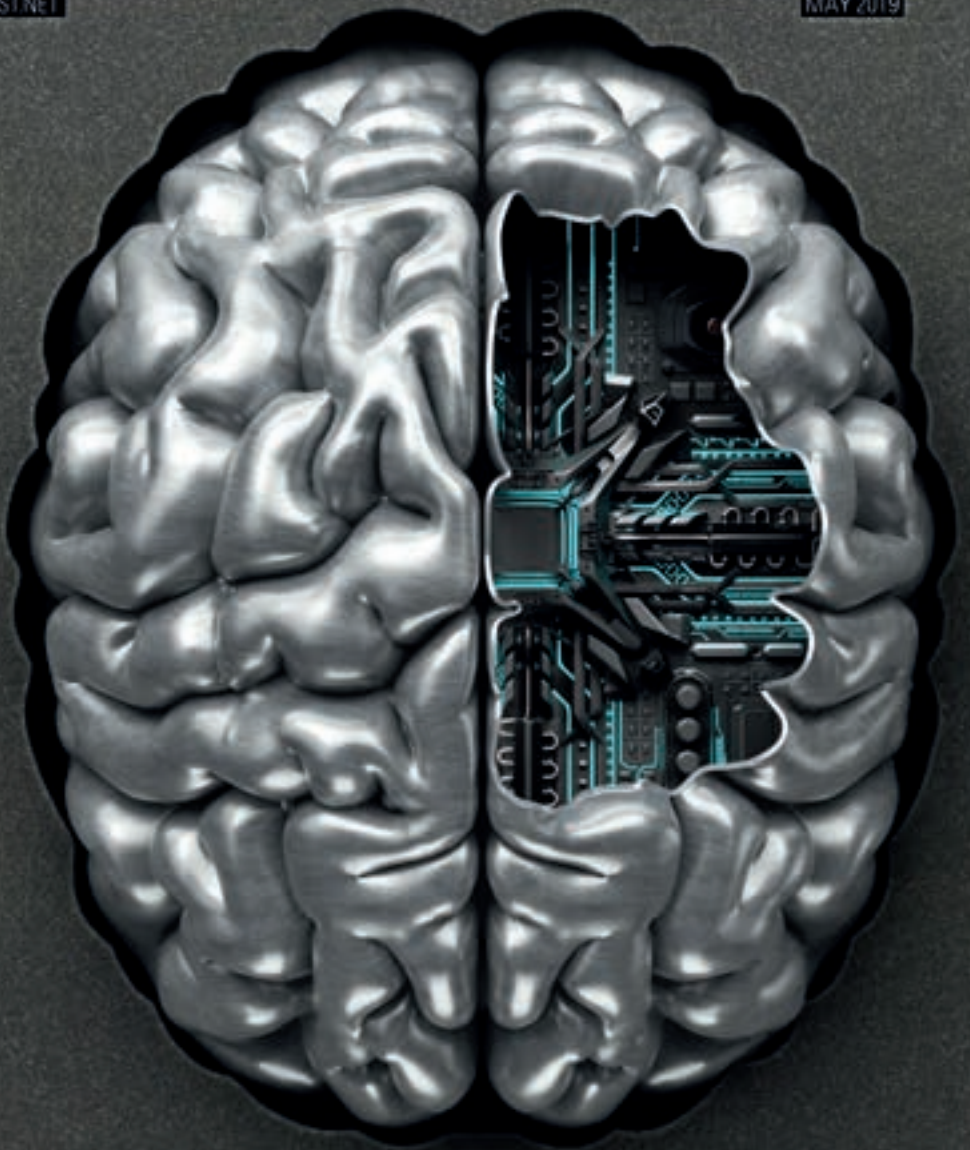
THE BIOMEDICAL SCIENTIST

THEBIOMEDICALSCIENTIST.NET

MAY 2019



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The rise of the robots: the impact of artificial intelligence on pathology

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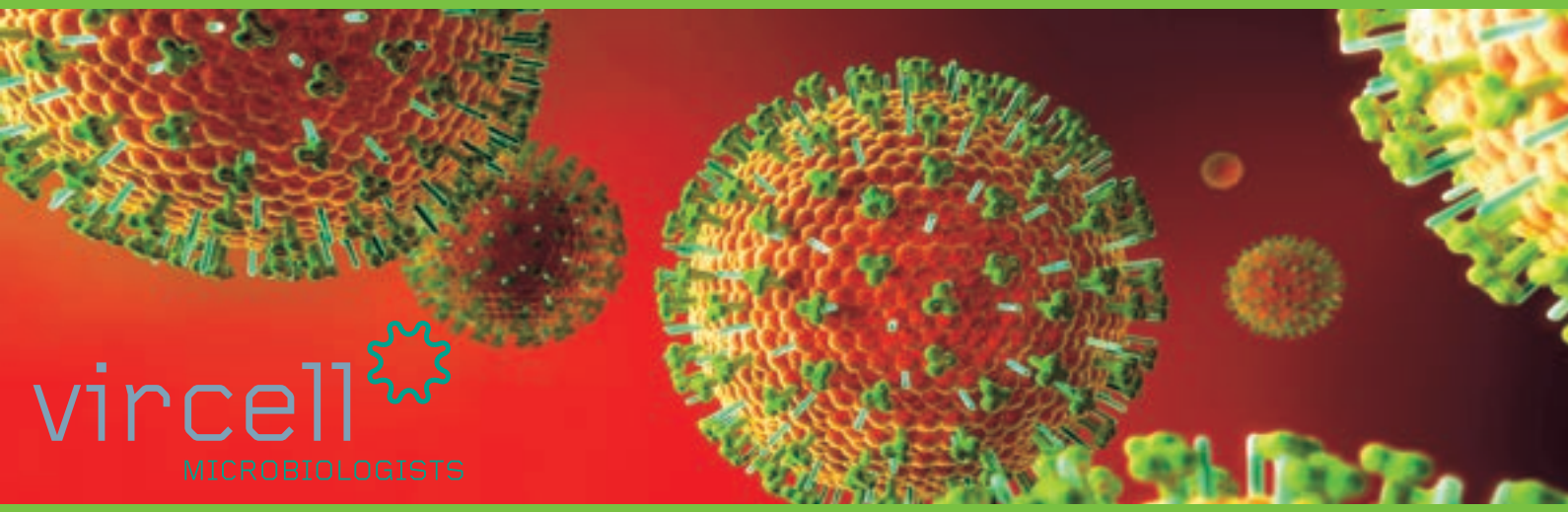

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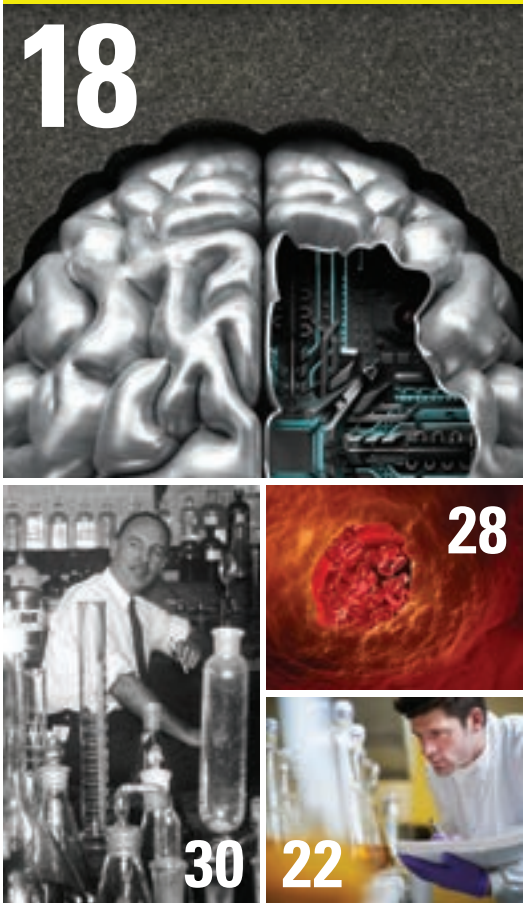

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PUBLISHING DIRECTOR
Aaron Nicholls
PRODUCTION
Rachel Young
DISPLAY ADVERTISING
James Rundle-Brown

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EQUALITY OF OPPORTUNITY

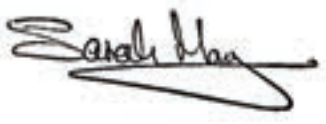
There is no place for outdated prejudice if there is a serious desire for change.

It is almost twenty years since biomedical scientists started to report abnormal cervical smears, an issue that divided medical opinion at the time, but which has proved to be a highly successful approach to managing a staffing and workload problem. From a biomedical scientist perspective, it was a development that has provided a valuable career extension to a small group of highly-qualified, competent and motivated individuals and which has opened the door to other individuals to take on roles that had previously been solely the preserve of medical pathologists.

The training of biomedical scientists to report histopathology samples is slowly gathering traction, although it still rivals Brexit in terms of division of opinion. I respect those in the RCPath who can see the staffing and workload cliff edge we are motoring towards; a recent histopathology survey that showed 25% of pathologists are over the age of 55 and the number of trainees entering the profession and completing training is dropping. Against the backdrop of a well-anticipated increase in the number of over 65s, many with multiple complex health needs, we have a situation that requires urgent action and also change.

I know I have written on many occasions about the opportunities for developing the biomedical scientist workforce but I am hearing more and more high-level discussions, both from within the professions and also at government department levels, about the need to be more flexible and creative. This is not coincidence, this is the dawning recognition that professional protectionism is not the solution. I have been aware for some time that the division between biomedical and clinical scientists in pathology is becoming less political and more practical. I am aware that language is softening and the collective term "scientist" is being used to denote an openness of opportunity that is based on merit and ability. Small but highly significant steps.

Biomedical and clinical scientists are professional groups with both distinction and overlap between their respective roles; while there is also a significant knowledge sharing between scientists and pathologists, the roles of the scientist workforce are not, and never will be, synonymous with those of the medically qualified. If pathology is to accommodate an increasing medical workload then a degree of pragmatism must be applied and the potential for the biomedical scientist workforce must be recognised – across all disciplines, not just within histopathology. I passionately believe that if pathologists accept that there are some aspects of their workload that could be undertaken by a scientist, there must be equality of opportunity where equality of ability and achievement can be demonstrated. There should be no place for outdated professional prejudice if there is a serious desire for change.



Sarah May
Deputy Chief Executive

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London, EC1R 5HL
United Kingdom
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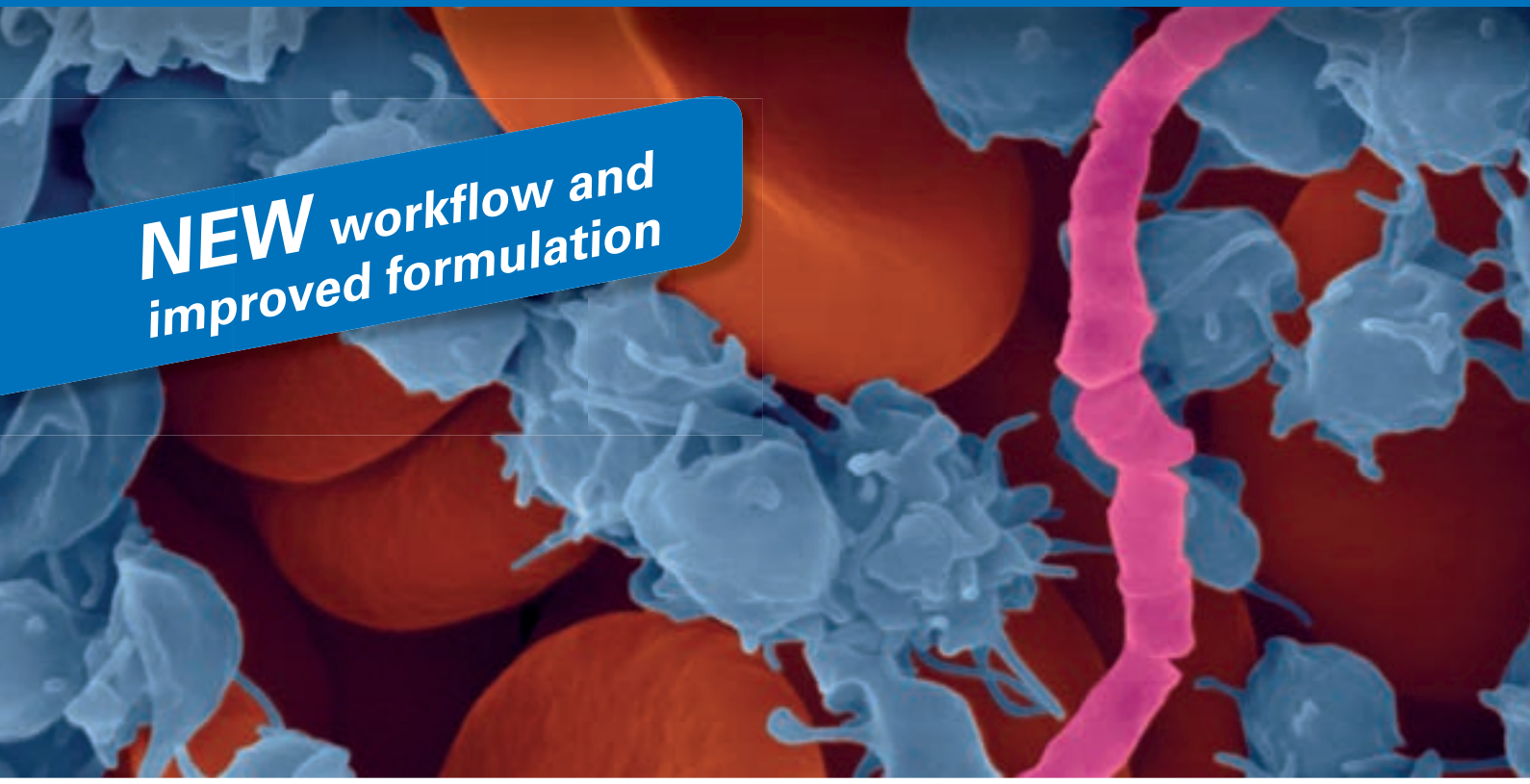

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SCIENCE NEWS

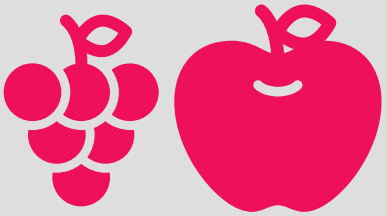
IN NUMBERS

11 million deaths

A new global study published in *The Lancet* says that poor diet is a factor in one in five deaths around the world.

3m

The dangerous diets are those containing:
Too much salt - three million deaths
Too few whole grains - three million deaths
Too little fruit - two million deaths.
Low levels of nuts, seeds, vegetables, omega-3 from seafood, and fibre are the other major killers. About **10 million** out of the **11 million** diet-related deaths are due to cardiovascular disease.



550

The Pint of Science festival involves 550 scientific talks taking place in UK pubs.
Nearly **400 cities in 24 countries** around the world are taking place. In London, there will be **35 talks held at six pubs,** including one dedicated to biology, medicine and health. The festival takes place on **20-22 May**. For more information visit: **pintofscience.co.uk**

21

Up to 21 young victims a day are treated in hospital after being wounded in knife or weapon attacks, according to new data.
The figures, released under Freedom of Information laws, show nearly **8000 people** aged **11 to 25 years old** attended hospitals with injuries gained **after assaults with weapons**.

500,000

UK and Chinese researchers, who followed **500,000 Chinese people for 10 years**, say that having one drink a day increases stroke risk. They found that one to two drinks a day increased **stroke risk by 10-15%** and four drinks a day **increased the risk by 35%**. Roughly **16 in 100 men** and **20 in 100 women** will have a stroke in their lifetime in the UK.

Three minutes

New figures show there's a diabetes diagnosis in England and Wales every three minutes.
Diabetes UK released its research that shows in 2017 **202,665 people** were diagnosed with diabetes across England and Wales – the equivalent to **23 people an hour**.

SCIENCE NEWS

PRE-ECLAMPSIA

Blood test for pregnant women

A new blood test to check for the potentially life-threatening condition pre-eclampsia will be available to women in England.

NHS England is making placental growth factor (PLGF) testing more widely available to pregnant women, as evidence suggests it speeds up diagnosis.

Those who develop pre-eclampsia have dangerously high blood pressure, which can damage vital organs, but the condition can be managed if spotted early enough.

The PLGF test tells doctors if a woman is at high, medium or low risk, with those at higher risk closely monitored.

Trials of the new test, which costs about £70 per person, show it speeds up diagnosis, meaning life-threatening complications to mother and baby can be avoided.

More than 1,000 women at 11 UK maternity units took part in the trials during their second and third trimesters.

Using PLGF alongside regular blood pressure and urine checks cut the average time to diagnosis from four days to around two. Earlier diagnosis was linked with a lower chance of serious complications – 5.3% versus 3.8% .

The NHS in Wales, Scotland and Northern Ireland could choose to offer the test too.

GENOMICS

"POVERTY LEAVES MARK ON GENES"

A new study challenges prevailing understandings of genes as immutable features of biology that are fixed at conception.

Previous research has shown that socioeconomic status is a powerful determinant of human health and disease, and social inequality is a ubiquitous stressor for human populations globally.

In this study, researchers found evidence that poverty can become embedded across wide swaths of the genome.

They discovered lower socioeconomic status is associated with levels of DNA methylation (DNAm) – a key epigenetic mark that has the potential to shape gene expression – at more than 2,500 sites, across more than 1,500 genes.

They state that this means poverty leaves a mark on nearly 10% of the genes in the genome.

Lead author Thomas McDade said experiences over the course of development can shape the genome's function.

→ **bit.ly/BS_NewsMay01**

HAEMATOLOGY

BLOOD CELL PRODUCTION INSIGHTS

A healthy adult makes about two million blood cells every second, and 99% of them are oxygen-carrying red blood cells.

The remaining one percent are platelets and the various white blood cells of the immune system.

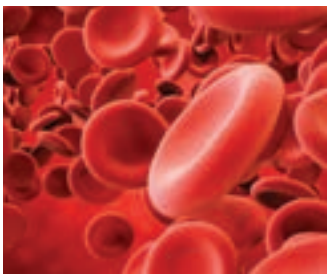
How all the different kinds of mature blood cells are derived from the same "haematopoietic" stem cells in the bone marrow has been the subject of intense research over recent years.

However, most of the studies have focused on the one percent – the immune cells.

Camilla Forsberg, a Professor of Biomolecular Engineering, said: "It is a bit odd, but because red blood cells are enucleated and therefore hard to track by genetic markers, their production has been more or less ignored by the vast number of studies in the past couple of decades."

Her team overcame technical obstacles to provide a thorough accounting of blood cell production from haematopoietic stem cells.

They state that their work is important for understanding disorders, such as anaemia, diseases of the immune system, and blood cancers, such as leukaemias and lymphomas.



One key finding is that all progenitor cells with myeloid potential are able to produce far more red blood cells than any other cell type.

This was surprising because many previous studies in which progenitor cells were grown *in vitro* found that they had limited capacity to produce red blood cells and platelets. Forsberg said those results now appear to be an artefact of the culture conditions.

→ **bit.ly/BS_NewsMay02**

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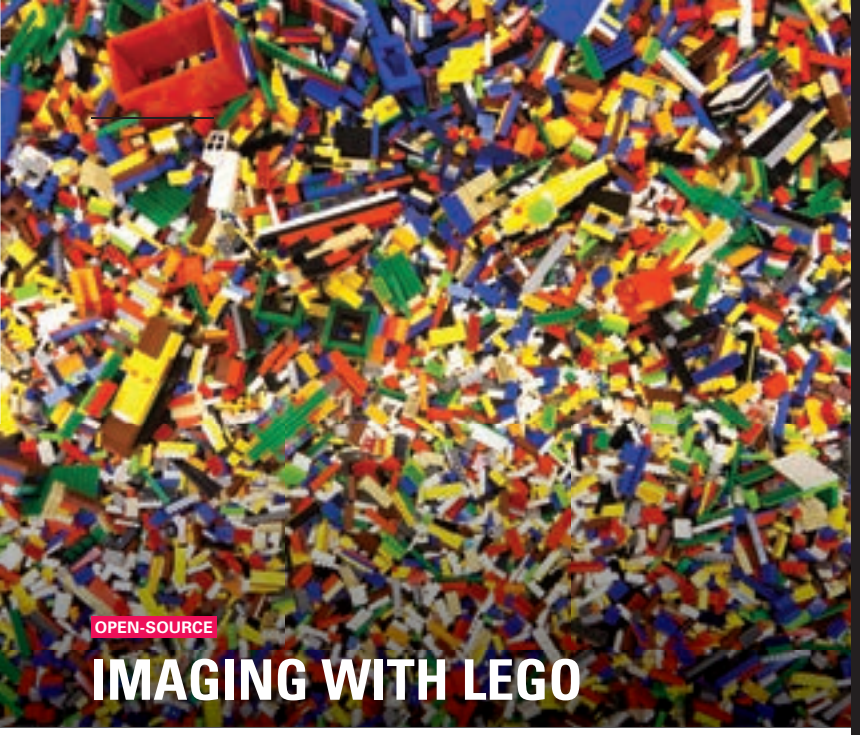


OPEN-SOURCE

IMAGING WITH LEGO

Researchers have come up with an inexpensive, automated way to image biological samples – using the children's toy, LEGO.

In a new paper scientists at the Crick, UCL and Aix University in Marseille describe a novel device, built with LEGO parts, that can be adapted to most microscopes.

Project lead Ricardo Henriques said: "Sometimes the best solutions to complex biological questions are remarkably low-tech. By developing hardware that uses inexpensive LEGO components as its building blocks, we've built an accessible tool that delivers customisable cutting-edge microscopy at a fraction of the cost."

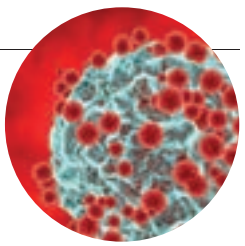
The device, called NanoJ-Fluidics (and nicknamed Pumpy McPumpface), enables researchers to observe cells in a highly customisable format. For the very first time, researchers can observe samples of cells at well-defined moments in time, for example when they are dividing or become sick.

The LEGO hardware and accompanying software are fully open-source, enabling other research groups to make their own devices. NanoJ-Fluidics has already been successfully adopted by over 10 labs across the world.

→ **go.nature.com/2GbGq0c**

HAEMATOLOGY

BLOOD TEST FOR RARE CANCER PROTEINS



A new blood test developed at the Johns Hopkins University can identify individual molecules in human blood samples with minimal detection errors.

Among the molecules was a mutated protein thought to be restricted to the inside of cells, mostly within the nucleus.

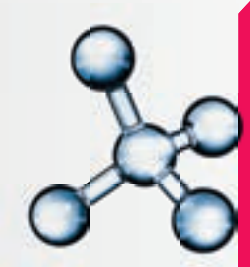
It is the first time that single-molecule imaging has been applied to visualise disease-causing molecules in blood.

The researchers call their new approach "single-molecule augmented capture".

They used the technique to detect rare intracellular proteins, secreted proteins and membrane proteins.

→ **bit.ly/BS_NewsMay03**

WHAT'S HOT AND WHAT'S NOT



HOT

ELECTRICITY

A "molecular surgery" process has been developed using tiny needles, electric current and 3D moulds to quickly reshape living tissue with no incisions, scarring or recovery time.

HOT

ZEBRAFISH

Research using zebrafish has revealed how key brain cells that are damaged in people with Parkinson's disease could be regenerated.

HOT

DIETARY FIBRE

Dietary fibre may be a new tool in the prevention of progressive lung disease, thanks to the production of anti-inflammatory short chain fatty acids, according to a new study.

NOT

LIGHT

Neuroscientists have linked white light at night – the kind that typically illuminates hospital rooms – to inflammation, brain-cell death and higher mortality risk in cardiac patients.

NOT

ZIKA VIRUS

Researchers have created molecules with strong anti-Zika virus potential. Their findings may also have an application in developing anti-parasite and antibacterial treatments.

NOT

STREAMS

A new paper looks at how faecal bacteria spreads in streams. Researchers assessed the dynamics of faecal bacteria on the basis of hydrological processes in the landscape and the connectivity of streams.

OBITUARY

MOLECULAR BIOLOGY PIONEER DIES

Sydney Brenner, one of the giants of 20th century science, has died.

He made many pioneering discoveries in the field of molecular and developmental biology, winning a Nobel Prize in 2002.

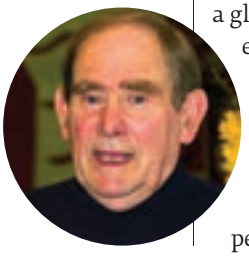
The award recognised his work with the tiny roundworm *Caenorhabditis elegans*, which is now widely used by researchers as a model to test the fundamentals of how all living organisms work.

But Brenner also made big contributions to the understanding of DNA.

He worked routinely with the other greats in this area, such as Francis Crick, François Jacob, Linus Pauling and James Watson.

Brenner helped establish the role played by the molecule RNA in carrying the "code of life" held in the DNA sequence to the ribosome protein factories in cells.

He also realised the significance of codons – the sets of three bases in the DNA sequence that signify the correct string of amino acids the ribosomes should use to assemble the proteins.



Born in 1927, Sydney Brenner famously taught himself to read from the newspapers that were used as tablecloths at dinner time.

At the age of 15 he won a scholarship to medical school.

BIOTECHNOLOGY

Breath testing for gut disorders

Small children may one day avoid invasive oesophageal tube-testing for gut damage and coeliac disease thanks to a new method.

It involves blowing into a glass tube to provide effective diagnoses.

In the first study of its kind, Flinders University researchers will trial the new dipeptidyl peptidase-4 (or "DPP4") breath test in a pilot study to measure a digestive enzyme found in the small intestine, which is associated with gastrointestinal damage and coeliac disease.

Lead researcher Dr Roger Yazbek said the specific DPP4 enzyme is produced in the small intestine and breaks down dietary proteins that have been associated with coeliac disease and associated gut damage.

He said: "This breath test represents a potentially new way to non-invasively measure gut health. Not only will these tests improve patient quality of life, but potentially save the health care system time and money, particularly if adapted for point-of-care testing in rural and remote areas."

→ **go.nature.com/2U912tE**

UNDER THE MICROSCOPE

This month: FAAH-OUT

I've never heard of 'FAAH-OUT" what is it?
It's the newly-coined term for microdeletion in dorsal root ganglia and brain-expressed pseudogene.

That's not a lot clearer...
OK – it's a mutation to a previously unidentified gene, which has led to a woman in Scotland feeling virtually no pain. She also experiences very little anxiety and fear.

How did they find this out?
At age 65, the woman sought treatment for an issue with her hip, which turned out to involve severe joint degeneration, despite her experiencing no pain. Then she underwent surgery on her hand, which is normally very painful, and yet she reported no pain.

What happened next?
Her pain insensitivity was diagnosed by Dr Devjit Srivastava, Consultant in Anaesthesia and Pain Medicine. She was then referred to pain geneticists at UCL and the University of Oxford, who conducted genetic analyses and found the mutation.

What dies this mean for her?
Cuts and burns go unnoticed (sometimes until she can smell burning flesh) and heal very quickly. She is an optimist who was given the lowest score on a common anxiety scale, and reports never panicking, even in dangerous situations, such as a recent traffic incident.

What are the wider implications?
The findings of the paper, which has been published in the *British Journal of Anaesthesia*, point towards a novel pain killer discovery that could potentially offer post-surgical pain relief and also accelerate wound healing.

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NEWS

HORIBA
REAGENT KIT

HORIBA Medical has announced the launch of a D-dimer parameter for its Yumizen G haemostasis range of instruments.

The Yumizen G DDi 2 reagent kit offers a key measurement and reference exclusion test for the diagnosis of deep vein thrombosis and pulmonary embolism. It can also be used for monitoring the progress and effectiveness of treatment of disseminated intravascular coagulation.

The kit is available for its full range of coagulation instruments which covers the needs of any lab.

→ **horiba.com**

ORTHO
MICROSLIDE

Ortho Clinical Diagnostics has received a CE Mark for its new technology for clinical labs,the VITROS XT MicroSlide.

The MicroSlide will offer clinical labs the ability to simultaneously perform two tests per slide from a single blood sample, for the first time. Tests often ordered together, such as cholesterol and triglycerides,can now be performed simultaneously.

It is claimed this will improve performance, save time and lab space.

→ **orthoclinicaldiagnostics.**

OXFORD GENETICS
GENE THERAPY

Oxford Genetics has received £6.5m of new investment in a syndicated round. This means it now has an undiluted,post-money valuation of £30.5m.

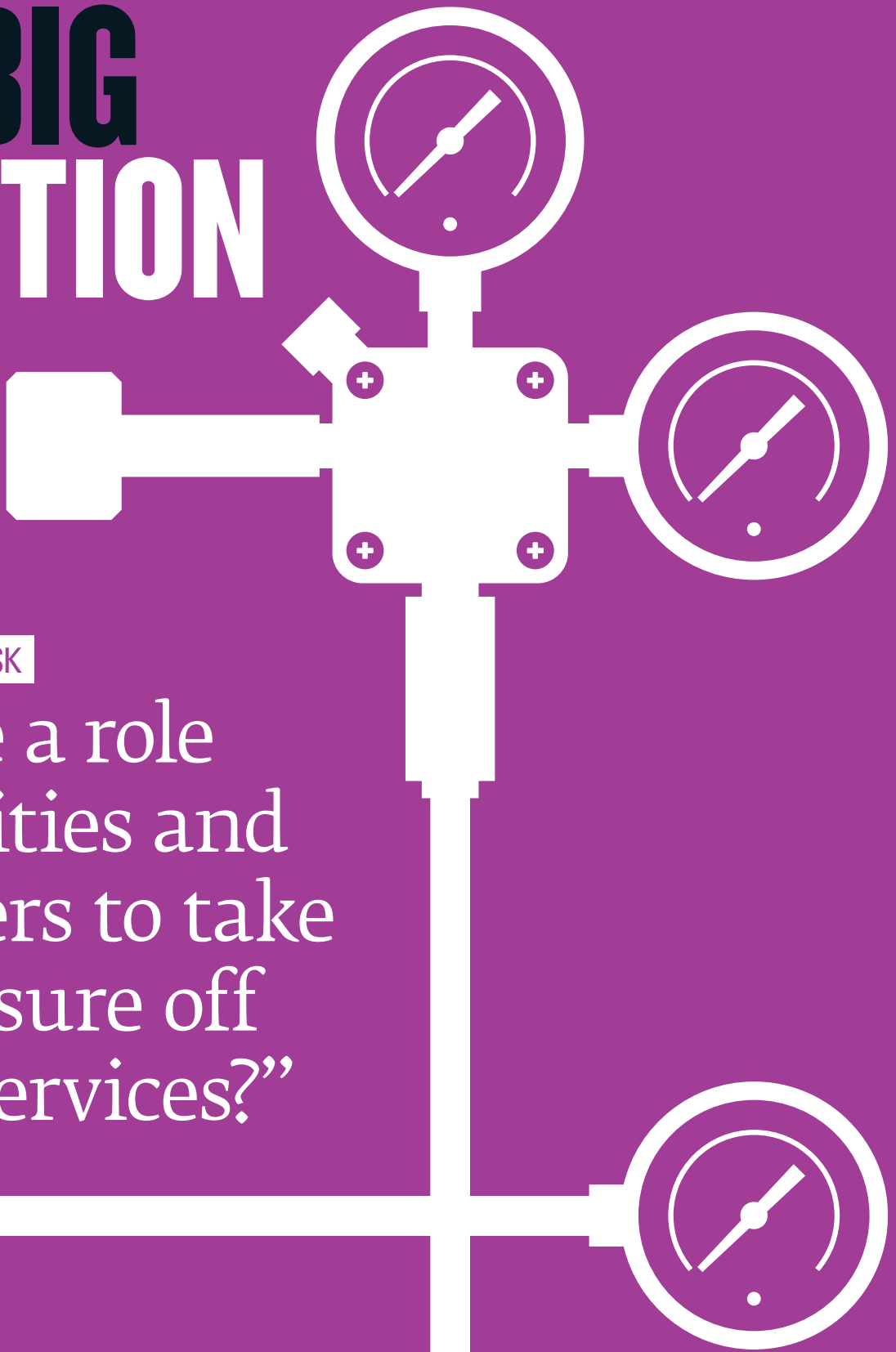
In the last 12 months,it has won six new licensing deals for its scalable gene therapy manufacturing.

Ryan Cawood,founder and Chief Executive,said: "Our customer base is shaping up to be an impressive collection of long-term partners and in addition,our increasing global reach is enabling us to further demonstrate our technical excellence and clear market differentiation."

The company offers a suite of solutions for gene therapy drug discovery, antibody therapy development and CRISPR gene editing.

→ **oxfordgenetics.com**

THE BIG QUESTION



THIS MONTH WE ASK

"Is there a role for charities and volunteers to take the pressure off health services?"

Colenzo Jarrett-Thorpe

National Officer for Health
Unite the Union

Trade unions in the NHS in England will shortly be publishing a charter with the Helpforce programme, which will provide certainty and clarity about the role of volunteers in the NHS in England, and a reference to NHS employing organisations, *Helpforce volunteers and their co-ordinators*, about how volunteers should be engaged and deployed in various health settings.

Trade unions have concerns regarding volunteering in the NHS around the use of volunteers undermining paid employed professions and occupations working in the NHS, including volunteers:

- should not undertake tasks that are instrumental in the journey of patient care and diagnosis
- should never be included in the employee numbers and should not wear the same uniforms and badges
- cannot be substituting for employed staff, to achieve safe staffing levels
- should not be engaged in tasks that impact on the registration or ethical conduct of employed staff
- should not be deployed to prevent the development of new roles in the NHS.

Also, the deployment of volunteers could lead to the blurring of lines with employed staff, impacting patient safety and confidentiality.

There has always been a role for volunteers in the NHS and the values of community activism, collectivism and altruism are shared in the trade union movement.

Bamidele Farinre

Specialist Biomedical Scientist
Great Ormond Street Hospital

Yes, there is. According to a recent report by the King's Fund, unpaid volunteers make a significant contribution to many departments across health and social care settings – contributing to the delivery of safe and equitable patient experiences.

Speaking from the viewpoint of a biomedical scientist, volunteer STEM ambassador and British Science Association Crest Award assessor, I can confidently say that the roles of volunteers and charities are vital and unprecedented. Charities and volunteers have been known to effectively and positively contribute to the NHS services as a whole, through devoting their time, energy and resources to promote continuous quality healthcare.

We are in an era where the needs of our ageing population continue to grow, and the NHS is under economic pressures to provide quality care for more people with limited resources, the greatest being staff shortages across the NHS. NHS leaders should be expected to take the role of volunteers and charities seriously and should endeavour to invest in them and integrate their services into organisations.

Staff are constantly short of time and it is a central part of the contribution volunteers make to the NHS: the extra pair of hands provided by volunteers enables staff to maximise the efficiency of their work, allowing them to deliver the clinical and specialised tasks they are trained to do.

Tony Dedman

Technical Lead for Biochemistry
South West London Pathology

There is the argument that if healthcare was properly funded and better utilised, there would be no requirement for the role of the various charities and volunteer workforce.

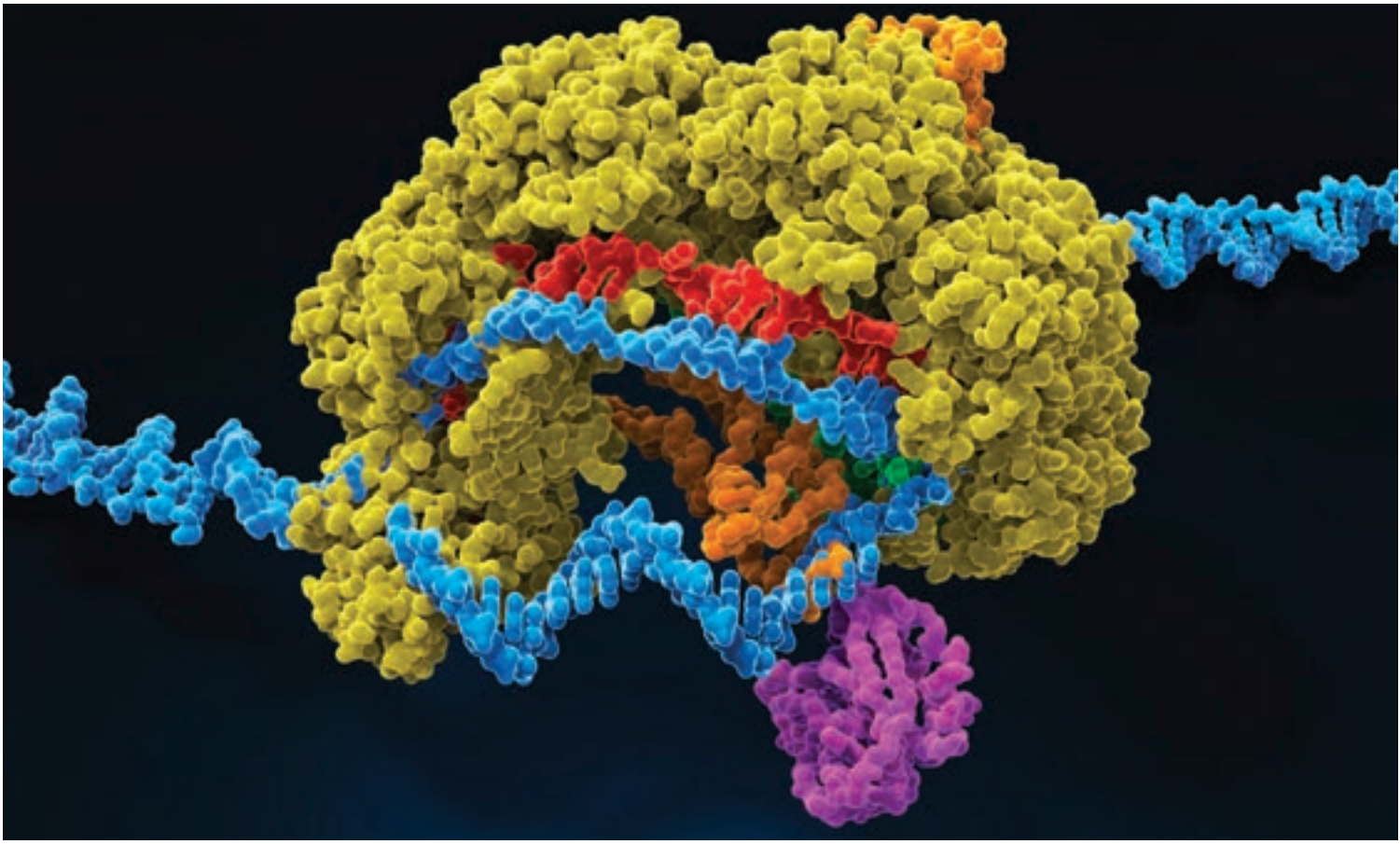
Many charities, regardless of size, provide additional funding for health services, which ultimately benefits the patient. Furthermore, if it was not for the many volunteers, the high street charity shops would not be viable economically with the resultant loss of funds, which would undoubtedly have a negative impact on patient care. It is these additional resources that ensure that lives continue to be saved.

Research is fundamental to the continued advancement of healthcare and if it was not for the support of charities, many research projects would never come to fruition. Many proofs of concepts and the resulting larger projects have been funded by charities, without which the latest treatments may have been unavoidably delayed.

The valuable work of the charities must not be overlooked, as they currently play a vital role in supporting many areas of the health services, both from a fiscal and from a manpower perspective.

The role of the volunteer in more clinical environments, such as helping to feed patients and providing companionship, is a different issue. What is their responsibility should a patient's condition deteriorate while they are getting fed? I am sure there is training, but I doubt it is substantive and it will not be repeated with adequate regularity.

MOLECULAR SCISSORS



Jennifer Doudna is behind a pioneering gene editing technique, potential applications of which range from curing genetic diseases, to improving crops. She discusses the practical and ethical issues.

The prospect of gene editing, or the process of changing and manipulating the DNA of a living organism, has been looming from the moment in 1953 when the double-helix pattern was discovered and described.

Small incremental steps towards making the technology a reality were replaced with a giant leap in 2012, when the teams headed by Jennifer Doudna, Professor of Chemistry and Molecular and Cell Biology at the University of California, Berkeley, and Emmanual Charpentier, then Professor at the Laboratory for Molecular Infection Medicine in Sweden, perfected the gene-editing technique called CRISPR-Cas9.

CRISPR is the acronym for "clustered regularly interspaced short palindromic repeats", and Cas9 is the CRISPR associated protein 9, which is an RNA-based enzyme used to make specific cuts to the DNA. Cas9 was developed in the wake of the discovery that certain bacteria in the immune system could fend off invaders by slicing up their DNA.

"CRISPR harnesses a naturally

occurring defence process that bacteria use to fight viral infection," says Jennifer Doudna. "Like a pair of molecular 'scissors', CRISPR enables researchers to make precise changes to the DNA of virtually any organism. We can do this because Cas9 can be programmed with a short piece of RNA. The sequence of DNA that gets cut can be easily changed by changing this short piece of RNA. The technology may allow us to cure genetic diseases, enhance drug development, reprogramme immune cells to fight cancer, improve transplant organs, and produce even more nutritious crops."

So the advantage of CRISPR-Cas9 is that it's a relatively simple, clean and precise method for editing genes. But this accessibility and comparative ease of use also presents a problem, as was shown last year when a Chinese scientist – Dr He Jiankui – said that he had injected two embryos with CRISPR technology in a bid to make them HIV resistant. Condemnation was swift and united, with one of the key voices belonging to Doudna. Through her work in developing the technique, she has become deeply aware of its potential for transforming health and society, and highly concerned for its ethical application.

In the light of recent developments, what are her thoughts on the ethics of editing genes? "CRISPR-Cas9 is entering legitimate clinical trials that could lead to cures for sickle cell disease and blindness in individuals, and 2019 will likely see an acceleration of this amazing progress," she says. "Though we should be mindful not to over-regulate, the global community needs to work together to ensure that advances come as safely and quickly as possible while respecting ethical boundaries.

"Nearly all of the current efforts to use CRISPR-Cas9 in humans involve somatic cell editing: changes to DNA that affect just an individual and are not heritable. But a major issue has been if, how and when to use CRISPR for germline editing: changes to DNA in embryos, sperm or eggs that are then passed down to other generations. In the US, the 1995 Dickey-Wicker Amendment prohibits human germline editing, and the National Institutes of Health are forbidden to fund any such research. The practice is banned in many, but not all, countries. At this stage, I support the plans of WHO and the National Academies to recommend strict regulation that preclude use until scientific and technical questions are addressed, and until ethical and societal matters are resolved. But open discussion and transparency around this important topic should be encouraged."

In the meantime, what should researchers be doing? "They must stick to sensible boundaries and avoid unintended consequences," says Doudna. "To have a reasonable discussion, we must focus on asking how do we ensure the safety of embryo editing, what diseases or genetic conditions should we allow to be edited out of our germline, how will access to this technology impact society, and how do we engage in active and informed public discourse? Right now, germline editing does not pass even the simplest of those tests – safety – so researchers should not be editing embryos for implantation."

What do we know about the risks and other possible side-effects? "Like any experimental technology, we are learning about unforeseen issues and trying to solve them through continued research efforts. Rigorous pre-clinical testing in cells and animal models is key to uncovering any unpredicted issues before moving to human patients. The issues that we have seen so far are surmountable, and do not detract from the power and potential of the technology."

It's that power and potential of gene editing that has so many people excited. Beyond the vast scope of healthcare applications, the technology is also being used in other sectors, such as agriculture, and might even revolutionise construction, where it's suggested it could pave the way to self-repairing building materials. More immediately, what does Doudna think gene editing will achieve in the next decade or so?

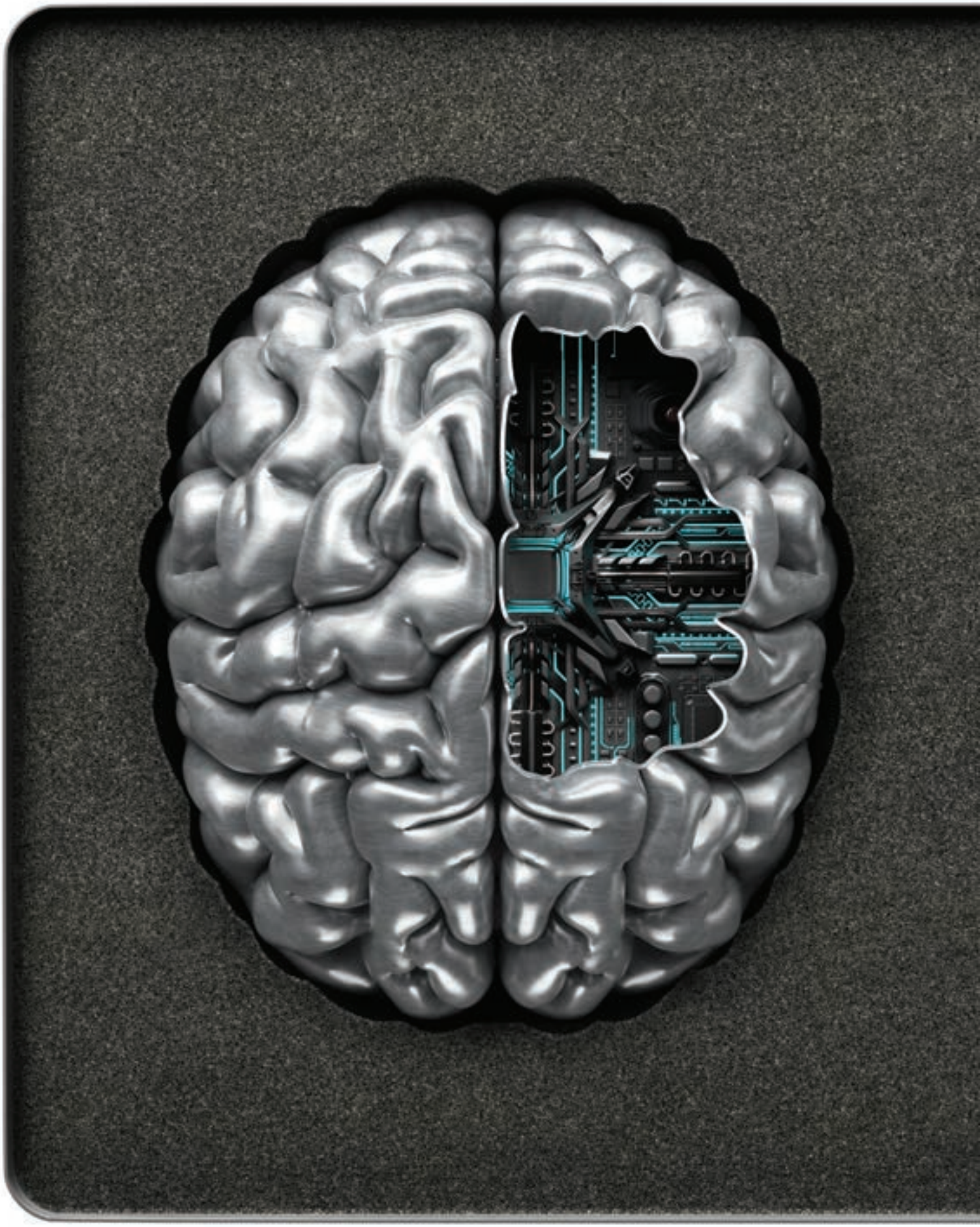
"Human applications particularly interest me, since CRISPR technology can take drug discovery and development to a higher level. Within the next 10 years we could see therapies for blood diseases, such as sickle cell disease and various eye diseases. In cancer, scientists are attempting to harness CRISPR to edit a patient's T cells so that they can target a particular type of tumour.

"For non-human applications, researchers are applying CRISPR to engineer pest- and disease-resistant and anti-browning crops, protect trees from bark beetles, and explore the possibilities of 'gene drives' to control mosquito populations and reduce their ability to spread Zika virus and malaria." BMS

JENNIFER DOUDNA

- ✔ Degree in chemistry from Pomona College, California, 1985.
- ✔ Worked at Harvard University under Nobel Prize-winning biochemist Jack Szostak.
- ✔ Completed a PhD in 1989, carried out postdoctoral studies at the University of Colorado.
- ✔ Joined the faculty at Yale University in 1994.
- ✔ Became Professor of Biochemistry and Molecular Biology at UC Berkeley in 2002.
- ✔ Her many honours include the Kavli Prize, the Breakthrough Prize in Life Sciences, the Heineken Prize, the BBVA Foundation Frontiers of Knowledge Award, and the Japan Prize. She is also a foreign member of the Royal Society.

IMAGES: SCIENCE PHOTO LIBRARY



THE RISE OF THE ROBOTS

Artificial intelligence is here. But what impact will it have on laboratories? Will it empower pathologists, or lead to a decline in the profession? We look at the issues.

For decades the debate has raged about "the rise of the robots". Looking back almost 150 years, we come across an early depiction of artificial intelligence (AI) in Samuel Butler's 1872 novel *Erewhon*, which features highly advanced robots with "human-like intelligence". Since then, in some permutation or other, utopian and dystopian visions of a future populated by robots have abounded. Now we are living in an age where AI is no longer a metal-clad vision on a distant horizon, it is the reality.

From online Amazon shopping recommendations, to Facebook image recognition, our everyday life is filled with real-world applications of AI. In some cases, the birth of AI has led to decline in other areas. For example, the surge in sales of AI-driven smartphones has led to a 50% drop in landline use in the past five years. While interactive maps on these devices have also led to a slump in A-Z map retail. Is this the fate of pathology labs? Will a rise in AI lead to a decrease in the number of roles for pathologists?

"Absolutely not," emphatically states Hamid Tizhoosh. "Any computer vision and AI algorithm can only help pathologists to do their job faster and with more confidence." It's a subject close to his heart, as a Professor of Systems Design Engineering and co-author of the recent paper "Artificial Intelligence and Digital Pathology: Challenges and Opportunities".

"We will always need the pathologist in the loop to generate labelled data for training, to validate the results, and write the report," continues Tizhoosh. "Besides, we have shortage of pathologists in many countries, remote regions, and undeveloped countries. AI can only assist pathologists to be more efficient and reach decisions faster and with more confidence."

IMAGES: GREG MEESON/HITANDRUNMEDIA.COM

Digital laboratories

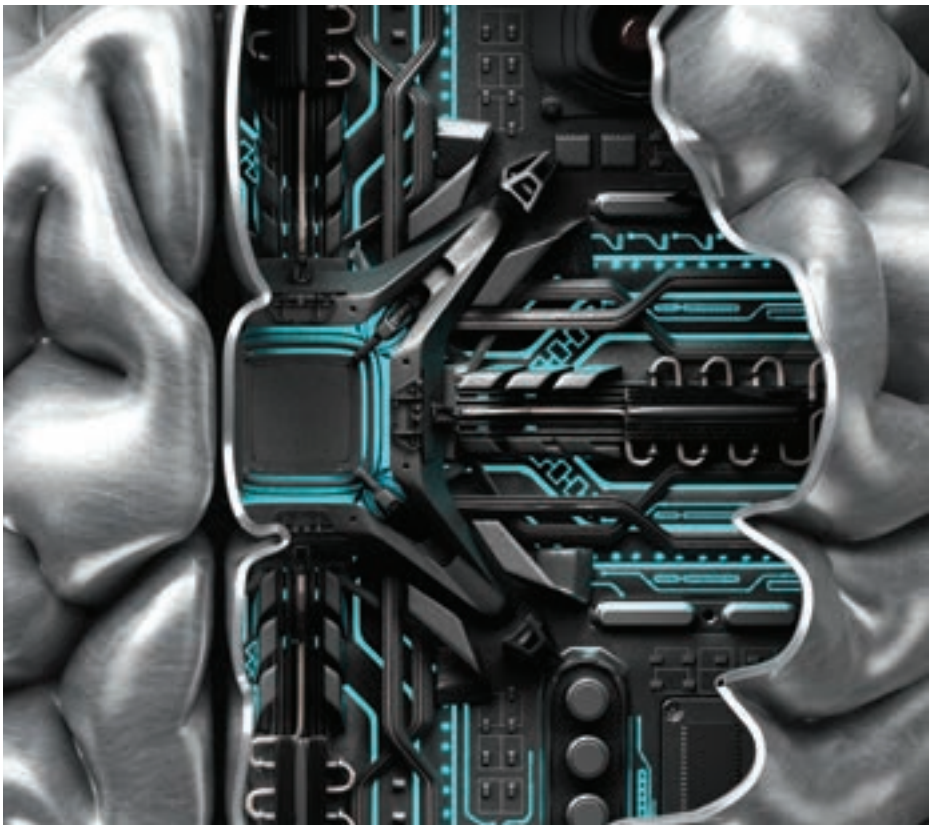
That is not to say that he doesn't see AI having an increasing role in labs. In fact, he believes "going digital" and the uptake of whole-slide imaging are inevitable. "Definitely, there is no doubt about that," says Tizhoosh. "However, it may still take some time, and the digitisation of pathology may occur with different penetration and speed in different settings and applications (teaching hospitals *vs.* private clinics and diagnostic *vs.* forensic pathology, for example).

"Admittedly, due to requirements of tissue preparation and the definitive nature of diagnosis in laboratory medicine, pathology is quite different from radiology. Nonetheless, many parallels can be observed, predominantly the generation gap in the user acceptance, workflow challenges, and costs for going digital are all factors that we already experienced when radiology abandoned films to embrace digital displays."

A histopathology lab in Leeds was the first of its kind to go 100% digital last September. Eight months on, Chloe Lockwood the biomedical scientist lead for digital pathology, says that the systems are bedding in well. "Since starting our 100% slide scanning, we have scanned just over 170,000 slides," she says. "The lab staff have really got to grips with the workflow and are enjoying using new equipment and technology. Our pathologists have all started their validation and are working their way to diagnosing digitally."

Any change brings resistance and the Leeds histopathology lab was no exception.

"There was reluctance, but not to the extent that they didn't want the change," Lockwood says. "There were concerns about the new ways of working, and how much impact adding digital pathology would have on their already busy work day. It's human nature to be reluctant to change, that's why it was important to make sure all lab staff were guided through the entire change process and digital pathology deployment and address any concerns that they had."



"This is something that will take away any menial work and will allow them to work more efficiently"

Benefits realisation work is currently underway to look into the tangible results and outcomes of the change, with a report due later this year. But Lockwood states that the anecdotal evidence suggests that lab staff are "getting back to basic histology" and the roll out has meant it has been possible to analyse overall workflow and "make improvements to streamline our histopathology process, whilst incorporating an additional scanning step".

Mundane tasks

She adds that she believes AI has a potential role in any task that makes a pathologist's work easier, such as cell counting. "Tasks like these, to a pathologist, are repetitive and a misapplication of their specialist knowledge. But given to a biomedical scientist with the aid of AI, the scientists are liberated and allowed to perform more complex tasks that they are capable of."

The topic was one that was under scrutiny at the Medical Imaging Convention, held in Birmingham in March, where there was a theatre dedicated to two days of AI and machine learning discussion. The broad consensus across the sessions was that AI has great potential to free up scientists' time.

Piotr Giedziun, co-founder of Cancer Centre AI, was discussing his work on PathoCam – whole-slide imaging software that allows users to save, annotate and share pathology images while using their own microscope equipment.

"This is something that is very easy and something that everyone can do," he said. "[Pathologists] have spent a lot of time learning and they will definitely still have a role – this is something that will take away any menial work and will allow them to work more efficiently. We see this as something that empowers pathologists."

It is a point that is echoed in the *Topol Review* – an independent report that was commissioned by the Secretary of State for Health and Social Care to look at the digital training needs of NHS staff. It says: "A benefit of systematically implementing AI and robotics in the NHS will be the automation of tasks viewed as mundane or repetitive that do not require much human cognitive power."

The future

The report goes on to admit that the role of AI "will change over time, with robots becoming the 'hardware' that embeds, for example, machine-learning algorithms to perform a manual or cognitive task". However, it goes on to stress: "As machines increasingly make decisions, there are ethical, legal and societal questions that need to be addressed."

There are papers published on an almost weekly basis about the abilities of AI when it comes to medical and laboratory work. For example, research published in the journal *Scientific Reports* in March claimed: "Using recent advances in machine learning, a Dartmouth research team has developed a deep neural network to classify different types of a common form of lung cancer on histopathology slides at an accuracy level shown to be on par with pathologists".

The paper states that currently lung adenocarcinoma requires a pathologist's visual examination of lobectomy slides to determine the tumour patterns and subtypes, which is a difficult and subjective task. Using recent advances in machine learning, it says, the team developed a deep neural network to classify different types of lung adenocarcinoma on histopathology slides, and found that the model performed on par with three practicing pathologists.

Just a few weeks previous to this report, a study that was published in *The Lancet Oncology* "established for the first time that artificial intelligence can process medical images to extract biological and clinical information".

Hamid Tizhoosh says that while the future of AI shows much promise, machines that make autonomous decisions will not be found in labs any time soon. "The recent success of AI is almost entirely due to 'supervised learning' – the type of learning that works based on 'labelled' data prepared by the physicians (for example, highlighting/delineating cancerous regions in histopathology images by the pathologist)."

He continues: "The research community is slowly moving toward 'unsupervised' AI, which is understood to be a more general and capable imitation of human intelligence. Those ideas, however, are clearly in their infancy. For the foreseeable future, AI will be closely supervised, and even for that we have not yet established all the regulatory rules."

While AI is now here – intrinsically embedded in our lives and increasingly in our labs, the debate on its role in healthcare services is far from played out.

The long-term future remains unknown, but the current view is that the patient and the workforce should be at the centre of any advances. As the *Topol Review* states: "Patient benefit must remain the driving criterion for AI and robotics design and use, and the workforce must be confident in its decisions about when and how human interaction must take priority over AI-human interaction." BMS

JARGON BUSTER

Artificial intelligence: The simulation of human intelligence processes by machines, especially computer systems. These processes include learning (the acquisition of information and rules for using the information), reasoning (using rules to reach approximate or definite conclusions) and self-correction.

Algorithm: An unambiguous specification of how to solve a class of problems. Algorithms can perform calculation,data pr ocessing,autom ated reasoning,and other tasks. The concept has existed for centuries and Greek mathematicians used algorithms for finding prime numbers.

Machine learning: The scientific study of algorithms and statistical models that computer systems use to effectively perform a specific task without using explicit instructions,r elying on patterns and inference instead.

Deep learning: An AI function that imitates the workings of the human brain in processing data and creating patterns for use in decision-making. Deep learning is a subset of machine learning that has networks capable of learning unsupervised from data that are unstructured or unlabelled. Also known as deep neural learning, or deep neural network.

Big data: A term to describe a large volume of structured, semi-structured and unstructured data that have the potential to be mined for information and used in machine learning projects and other advanced analytics applications. Big data are often characterised by the 3Vs: the extreme volume of data, the wide variety of data types and the velocity at which the data must be processed.

50 YEARS OF MONITORING QUALITY

To mark the half a century of UK NEQAS, three members of its consortium outline its growth from a short-term, UK-focused project in 1969 to the internationally-recognised organisation it is today.

Dr Mitchell Lewis

At a recent UK NEQAS Haematology annual meeting, approximately three-quarters of the audience of 300 admitted that they had bought, borrowed or used a copy of *Dacie and Lewis Practical Haematology*. This book, now in its 12th edition, has been a mainstay in the haematology library and it is difficult to imagine working life without its clear instruction. Dr Mitchell Lewis was a clinical haematologist at the Hammersmith Hospital in London, who remained firmly rooted in the laboratory and understood the importance of reliable and accurate laboratory results in treating patients. His original work in the 1960s focused on the measurement of haemoglobin – possibly the most frequently requested test in pathology, but one that we did not always get right.

The award in 1968 of £3,000 a year from the Nuffield Provincial Hospitals Trust for a three-year project, intended to harmonise haematology laboratory performance throughout the UK, led to the foundation of UK NEQAS Haematology in 1969.

Dr Lewis also co-founded the International Council for Standardisation in Haematology (ICSH) and was committed to the improvement in laboratory standards in resource-challenged regions of the world, working in collaboration with the World Health Organization (WHO) on guidelines for the operation of EQA programmes.

Professor Tom Whitehead, CBE

Having delineated a rigorous approach to quality control in a period when manual assays for clinical chemistry analytes gave way to highly automated processing for large panels of tests, Professor Tom Whitehead turned his attention to between-laboratory agreement. Initial comparisons between

laboratories at the Queen Elizabeth and General hospitals in Birmingham led to wider reviews across the West Midlands. A grant of just £500 from the then Ministry of Health enabled inception of the National Quality Control Scheme for Clinical Chemistry, with its first distribution in July 1969. This two-year project (somewhat optimistically intended to "resolve all issues, so it could then be stopped") established the basic principles of EQA, including scoring of performance.

Development of the UK NEQAS network of programmes was then overseen under Tom's chairmanship of the Department of Health's Advisory Committee on Assessment of Laboratory Standards (ACALS), including WHO's adoption of the term external quality assessment rather than "control" for the activity. Tom travelled extensively to promote the establishment of internal and external schemes internationally, including schemes in Myanmar (Burma), Korea, Mexico, the Middle East, Thailand and Zimbabwe. He encapsulated his ideas and philosophy in his widely acclaimed book, *Quality Control in Clinical Chemistry*.

The UK NEQAS organisation today

UK NEQAS now offers more than 140 schemes from 24 specialist UK centres across all pathology disciplines, hosted primarily by NHS trusts but also including Public Health England, universities and other "not-for-profit" institutions. The central UK NEQAS charity designates UK NEQAS members, subject to the UK NEQAS Code of Practice, but the charity neither directs the operation of the schemes nor employs their specialist staff. All UK NEQAS schemes are self-funding, operated on a strict not-for-profit basis and independent of external bias or commercial interests in laboratory equipment, reagents and services. The core UK NEQAS principle remains the improvement of laboratory performance through education. Data from UK NEQAS schemes provide 'state of the art' assessments of equipment and reagent performance, contribute to the evaluation and standardisation of methodologies and the development of high-quality, evidence-based guidelines in laboratory medicine.

Innovation in EQA is an area in which UK NEQAS has always led. Our EQA services include quality assessment of the "end-to-end" process of patient investigation, including interpretation of results either in standalone programmes or integrated into standard exercises.

Through PrepQ, UK NEQAS has established a true end-to-end quality

monitoring service, allowing laboratories to monitor pre- and post-analytical issues and supporting the requirements of ISO 15189. In point-of-care testing (POCT), UK NEQAS is at the forefront in establishing EQA for the myriad of near-patient devices available globally and this will form a key part of EQA programmes in the future. A final major area of work is the development of genomic testing EQA to support the 100,000 Genomes Project and the NHS England National Genetics Testing Catalogue, where UK NEQAS was selected as the sole EQA organisation able to provide the robust, high-quality EQA necessary to support these initiatives. This led to the rapid development and implementation of bespoke EQA programmes for specific aspects of genetic testing, from DNA extraction to the detection of translocations and point mutations – ensuring that the data produced from genomics testing are fit for purpose.

Evolving diagnostic pathways mean that a single patient journey will involve multiple healthcare scientists across a variety of specialties. As a result, the first Pan-UK NEQAS International meeting will be held in Dublin in November 2019, featuring a multi-disciplinary programme, in addition to our specialty-based participants' meetings. We are also attending EuroMedLab 2019 in Barcelona in May, allowing more international scientists to interact with the UK NEQAS team. Finally, we have several dedicated UK NEQAS sessions at this year's IBMS Congress to discuss the role of EQA in laboratory diagnostics.

A day in the life

UK NEQAS packages are a familiar feature of laboratory life, regarded either as a nuisance, an exercise to comply with ISO 15189, something "only senior staff do", or an interesting challenge and educational opportunity. The packages arrive from a disembodied Post Office box address, results are entered and reports downloaded electronically, thus reducing the need for human interaction. Common factors are that specimens may turn up the day after you have done the assay or when staff are scarce, specimens are too small or the closing date too short for your regular processing. However, the vast majority of laboratories experience no such problems and greatly value the personalised assistance they receive if they do have to contact the schemes. The sheer scale of the operation behind your individual package may not be apparent to most. A single UK NEQAS Haematology distribution, for example, uses over five litres of whole blood, takes up to three months' planning and results in more than 1,000 packages for distribution, with 120 different combinations of specimens; practices that are reflected across each UK NEQAS centre.

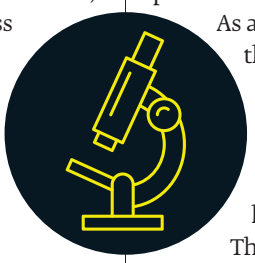
We have several NEQAS sessions at IBMS Congress to discuss the role of EQA in lab diagnostics

The future

In common with our participants, we face challenging times. The pathology landscape in England is changing with the advent of pathology networking and consolidation; practices that are repeated in many other health economies. Currently, the proposed hub and spoke networks are in development and NHS Improvement intends to meet with UK NEQAS to discuss the potential for new or modified EQA systems that will be required by the new networks.

UK NEQAS remains an essential component of laboratory medicine clinical governance, providing education, facilitating clinical audit, monitoring clinical effectiveness, assisting in the management of risk, and generating information used for research and development. Oversight of individual laboratory performance is supported by the Joint Working Group on Quality Assurance and its associated National Quality Assurance Advisory Panels, directly influencing patient care. Participation in EQA is a requirement for laboratory accreditation to ISO 15189 and for many investigations UK NEQAS is the sole or preferred EQA provider. UK NEQAS also works to develop services to support NHS objectives (for example through the National Screening Programmes) and is represented on committees, such as the Serious Hazards of Transfusion committee, that contribute significantly to national clinical governance.

At UK NEQAS we continue to be astonished at how far the organisation has developed and new staff are enthusiastic about how far they can take us in the future. However, we all work for the benefit of the patient and are proud to be a part of effective, high-quality healthcare provision in the UK and internationally.



As an organisation, we realise that there is much to be done to maintain and develop EQA systems in partnership with our participants and we welcome your contribution on how we can meet your needs. Thank you to all our participants and we hope that we can rely on your continued support for the next 50 years.

Barbara De la Salle, **David Bullock** and **Liam Whitby**, writing on behalf of the UK NEQAS Consortium.

TOP FIVE... CONGRESS TIPS

With just one more month of early bird discount rates for **Congress 2019**, we ask five regular attendees and previous speakers their top tips to make the most of Congress.

01 Sarah May

Deputy Chief Executive, IBMS

The programme is purposely scheduled so that all sessions end and start at the same time,m eaning you can pick and choose what you go to without missing the start or end of a talk. My tip would be that people do not µst confi ne themselves to their own discipline -look at what is on offer and take advantage of the opportunity to learn something different.

02 Diane Anderson

National Technical Training Manager, Scottish National Blood Transfusion Service

Read through the programme,plan your timetable in advance and try to attend at least three different disciplines. The format is often different,but you will be amazed at how the subþct m atter links into your existing knowledge. Also,m ake a point of visiting the exhibition -not µ st for the goodies or cocktails -but to see what advances in technology and diagnostics are available.

03 Ian Sturdgess

Pathology Services Manager, West Hertfordshire Hospitals NHS Trust

Fr stly,Iđ say enj oy yourself. Congress is a total learning experience and it's im portant to get the most out of that. We have the lectures for all disciplines,which ar e great,but it's also r eally important to go to the trade show and talk to the company representatives about their products. It's only by getting out ther e and speaking to people that you can learn what is possible.

Also,networ king -it's ver y useful to build up a network of colleagues who you can speak to in times of question or doubt. This wont happen over night,but Congress is a great first place to start.

04 Wendy Leversuch

Head of Scientific Training, Health Services Laboratories

Be prepared! Congress is busy and fast paced, it is crucial to know what you want to see and, more importantly, where everything is. I'm often crossing different disciplines and need to move fast to catch the next lecture. Never miss the exhibition -keeping up to date with what supplier s offer and what developments are happening is an important reason to visit. Dont µst hover ,go up and talk to people on the stands.

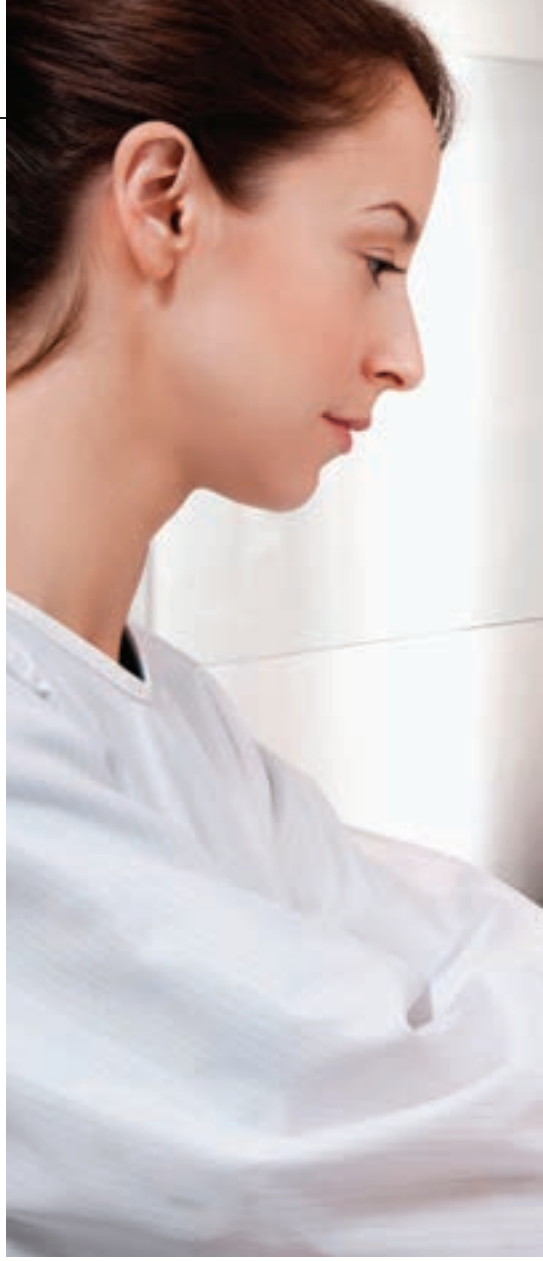
05 Pav Jheeta

Associate Practitioner and Project Co-ordinator in Microbiology, Sandwell and West Birmingham Hospitals NHS Trust

It's a ver y important event and while not everyone can afford to go for all the days,Iđ r ecommend people come along to whatever they can. With the way the NHS is changing and roles becoming more multidisciplinary,networ king is vital to strengthen your knowledge,put your self out there and learn about new advances and opportunities. My other tip is to be prepared in any lectures. It can be intimidating,but wr ite down any questions you have during the talk and dont be scar ed to ask them at the end.

REFLECTIONS OF A QUALITY MANAGER PT.2

Mairiead MacLennan takes a look at the validation, verification, variation and the uncertainty that surrounds these terms.



Confusion, concern and misunderstanding abound in discussions on validation and verification – two very different processes (they have two separate sections in the standard for that reason).

Evaluation can accompany either, which may be the source of confusion for some. To keep it simple, consider the following.

Before introducing a piece of equipment or new platform, the department decides, based on service needs and the task the platform must perform, which item they need/want from several options. Requirements might include that it must:

- Interface with the LIMS
- Fit in the space available
- Get through the front door, (or the door of the lab in which it will be used)
- Be possible to run specific kits currently being used
- Be validated to run that kit with their platform
- Achieve acceptable limit of detection
- Evidence that manufacturer's validation meets the needs of the department
- Demonstrate the process has been performed and described previously in a peer -reviewed article.

Brainstorming with colleagues will identify these requirements, which now become the acceptance criteria. It's never a good idea to set acceptance criteria after the item is installed. Prioritise the list. Evaluation is the act of performing the "test drive" of the platform and determining whether the acceptance criteria are met.

Verification

The laboratory is required to determine that the same output is achieved when operating *in situ*, as would be expected from their current test, using previously tested samples and/or from other material tested elsewhere. However, the laboratory must also have reviewed the information on the new kit/platform as a standalone, not just comparing it with the previous kit.

While testing or evaluating, the laboratory must ensure validation and CE mark. The expectation of performance must also be predetermined and these are the acceptance criteria of that kit/platform combination. The results of these test runs must be comparable to a high degree.

When doing exactly what is described in the kit insert, and using the platform as per the manufacturer's instruction, this is a verification, so long as the manufacturer's validation has been closely scrutinised during the review.

Validation

If, for example, the sample type the laboratory wants to use with the specified kit on the specified platform is not listed as validated on the kit insert, then a validation is required. Such novel work must, by its very nature, be more extensive and detailed, to take account of unknown variables in order to identify them as such. The process has usually not been performed and described previously in a peer-reviewed article. There may be more specimens required from a patient than would normally be taken, for example one each of the validated sample type and the non-validated sample type to be able to demonstrate that the test detects the target as well as (or even better than) the current method or other 'gold standard'. Validation demonstrates that an alternative , novel process gives valid results. Verification demonstrates that the laboratory can reproduce what the kit insert describes.

IMAGES: ALAMY

Uncertainty

Measurement uncertainty (MU) also causes consternation. It is concerned with determining, understanding and managing the inherent error or variation in any test that primarily involves measuring or counting something. The "something" can be anything and is called the measurand. For the cell sciences this has only become an issue since accreditation to ISO15189.

As recently as four years ago, well-respected experts in the field were still saying, "tell UKAS we don't do MU in microbiology and cell pathology". However, we most certainly do.

The most obvious examples of measurands for these disciplines are antibiotic disc measurements, cell counts, colony counts and tissue excision margin measurements, though there are more.

Variation

It becomes clear that the blatant very low counts or very high counts or measures, well away from the cut off, are not an issue. Around the critical level or decision-making values, the "error" or variation must be determined as accurately as possible. Any variation between and within operators must be established and importantly assessed for the impact on the results that the laboratory issues.

Sophisticated statistical analysis of the data is not necessary, nor actually, in my opinion, desirable. All operators must be able to understand what this MU means to their result output, so that if a result around a cut-off value is achieved, they understand the impact and the required action.

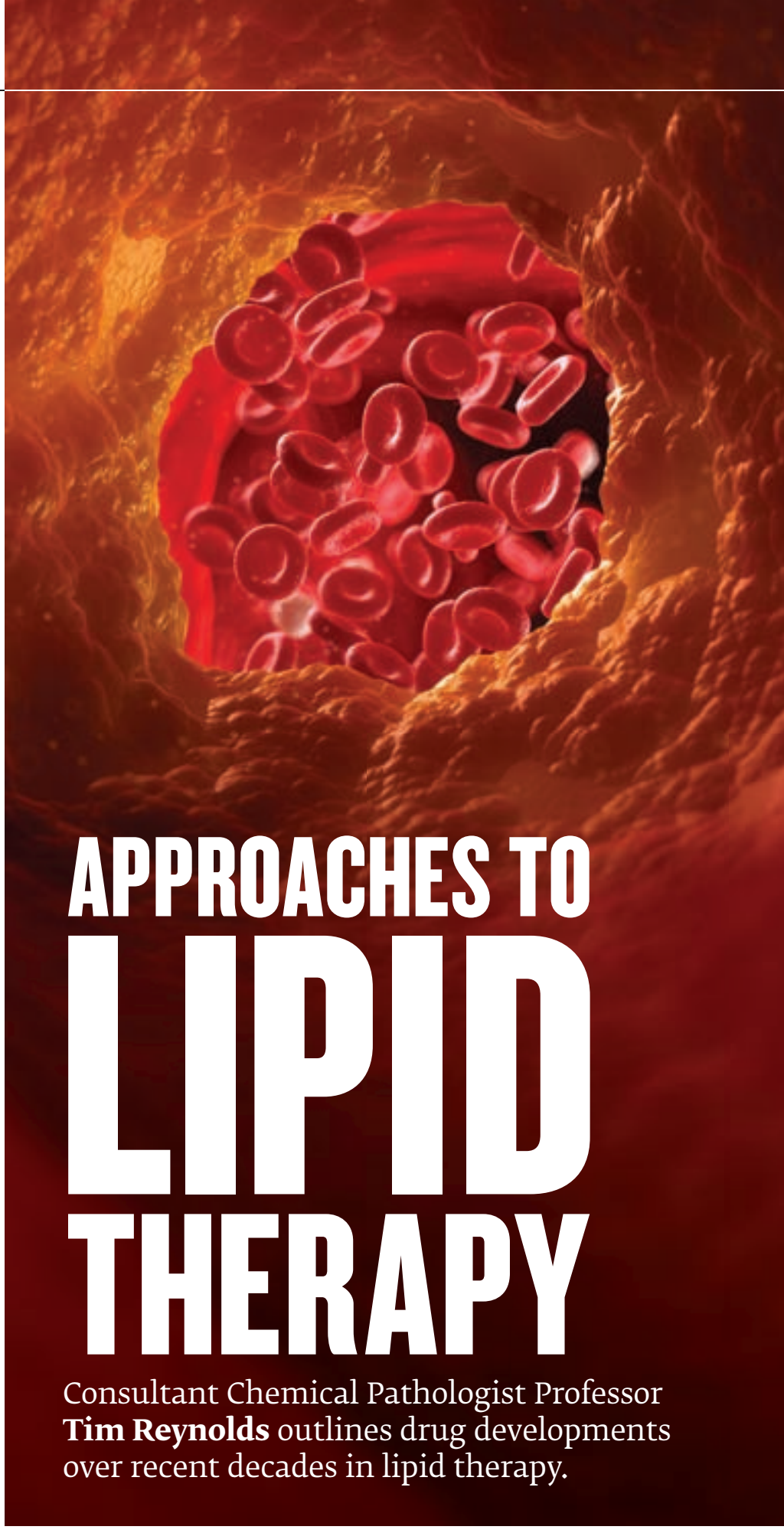
I have no doubt that reading this are those who do not believe that tests will give results in the critical range where some that could be positive on one "run" could be considered negative on the next, because the manufacturer wouldn't have set the test up to do that. I can assure them it does happen. In a PCR test with CT value cut off of 38, above which the result is deemed negative, it is entirely possible that a value of 37 might be achieved and, if run again, a value of 39. So, what is the "right" answer?

These are the areas in which values are important to reporting clinicians to permit appropriate interpretations. So the understanding of MU is vital when reporting such results. If a platform is set to interpret a result as positive or negative on a discreet figure, the team that understands the test, with the clinicians, must perform an impact assessment and establish policies on managing such results. A record of such a discussion based on verification data will provide evidence that measurement uncertainty has been established and the impact assessed and considered in relation to critical values when reporting.

Competence

Providing statistical data, which operators do not understand, can lull a laboratory into a false sense of security. If K factor or % CV are used to express MU, do all the operators in that laboratory, including clinical reporting staff, know how to apply that figure to the results? If not, the exercise is pointless. To demonstrate competence, a question on MU must be included in their training record, thereby closing the loop of knowledge understanding and application. This is what a Technical Assessor means when they ask if MU has been determined, applied and impact assessed. BMS

Mairiead MacLennan is Professional Manager (Quality and Training) at the Department of Medical Microbiology and Infection Control, Victoria Hospital in Kirkcaldy. She is also a Technical Assessor for UKAS.



APPROACHES TO LIPID THERAPY

Consultant Chemical Pathologist Professor **Tim Reynolds** outlines drug developments over recent decades in lipid therapy.

Statins were introduced in the early 1990s and, apart from the introduction of ezetimibe in 2002, have remained the mainstay of cholesterol lowering treatments. They work by inhibition of an enzyme: Hydroxy-methyl-glutaryl-coA reductase converts HMGcoA into mevalonic acid, which is the first precursor on the metabolic pathway that manufactures cholesterol. Ezetimibe works by inhibiting cholesterol absorption in the gut and was initially marketed as an adjunct to a weak statin (simvastatin) to make it as effective as a strong statin (atorvastatin). Both drugs work by reducing the availability of intracellular cholesterol in hepatocytes, which stimulates them to express more LDL receptors and thus remove more LDL from the circulation.

In drug development, a new class of drugs is introduced and, if superior, becomes the standard treatment. When either most drugs in that class have lost patent protection or a substantial research advance has been made, it becomes worthwhile for pharmaceutical companies to develop improved treatments using different mechanisms. This is seen in treatment for dyslipidaemia. The patent on atorvastatin ended in 2011 and that of rosuvastatin, the other very strong statin, ended in 2016.

In the last five years, HDL-increasing drugs working by the inhibition of cholesteryl ester transferase protein (CETP) have been developed, but clinical trials were disappointing. Torcetrapib was abandoned because the adverse event rate was too high. Trials of evacetrapib and dalcetrapib were abandoned for futility and the trial of anacetrapib showed that there was no significant benefit from CETP inhibition. A last ditch trial in genetically-selected individuals is being carried out for dalcetrapib, but this drug class looks doomed to failure.

PCSK-9 (properdin convertase subtilisin/

IMAGE: SCIENCE PHOTO LIBRARY

kexin-9) was discovered in 2003. It was found to be an important molecule in the regulation of cell surface LDL receptor numbers. The LDL receptor is responsible for capturing low-density lipoprotein particles from serum and allowing them to be taken up by the liver cell for metabolism. When an LDL particle binds to its receptor, the receptor is endocytosed into the cell. The endocytic vesicle has a lower pH than serum so the LDL particle is released and the receptor is recycled to the cell surface.

LDL receptors

If we have an old piece of equipment in our laboratories, we attach a destruction tag to it and the Estates Department comes and takes it to a skip; PCSK-9 has a similar function for LDL receptors. When the liver manufactures new LDL receptors, it also makes PCSK-9, which is released into the circulation. The PCSK-9 circulates in the blood and if it encounters an LDL receptor, it can bind to it. If an LDL receptor with a PCSK-9 bound to it is endocytosed, the receptor is not recycled back to the cell surface and is broken down in the lysosome along with the LDL particle it had captured.

This mechanism has important ramifications for patients with familial hypercholesterolaemia. In this dominant genetic condition, half of the LDL receptors manufactured by hepatocytes are affected by a mutation and do not bind to LDL, which results in high concentrations of cholesterol in the circulation, and subsequent ischaemic heart disease. PCSK-9 binds randomly to LDL receptors and will bind equally to functioning and non-functioning receptors. Receptors are endocytosed preferentially when they have captured an LDL particle, and functioning receptors will be removed if they have a PCSK-9 bound to them. This means that there is an alternative mechanism that can be used to increase cell surface receptor numbers. Instead of starving cells of cholesterol so they make new receptors, it should be possible to interrupt the removal of functioning receptors, thus increasing the number of receptors with a consequent decrease in circulating LDL.

There are several methods that can be used to reduce PCSK-9. The first of these, which has already entered clinical practice, following a NICE review in 2016, is removal of PCSK-9 from the circulation by binding it to a monoclonal antibody, which means it is not available to bind to LDL receptors. Initially, there were three pCSK-9 inhibitors in clinical trials, but bococizumab was discontinued because a substantial proportion of patients who tried it developed blocking antibodies because the molecule contained some sections of mouse origin, whereas the other two antibodies (alirocumab and evolocumab) are both fully human molecules. In the short time that these new agents have been on the market, they have proved extremely effective for patients with familial hypercholesterolaemia, with patients having reductions in LDL-cholesterol ranging from 20-80%. Many of these patients were statin-intolerant but have had minimal problems with PCSK-9 inhibitors and are, therefore, being treated effectively for the first time ever.

New methods

The problem with monoclonal antibody-based drugs is that they have to be given by injection and they are very expensive. A number of other methods of affecting the same PCSK-9:LDL receptor system are also being investigated. Some small molecule drugs that interfere with the binding of PCSK-9 to the LDL receptor have been created, but none have yet made it to clinical prominence.

There is, however, a further new type of drug that has been developed to target the PCSK-9 system: inclisiran is a small interfering ribonucleic acid (RNA) that inhibits PCSK9 synthesis. It is given by injection and is transported to the nucleus where it interferes with the expression of the *PCSK-9* gene by degrading mRNA post-transcription, thus preventing translation into protein. Early clinical trials have shown that it is effective when given at zero, three and six months and every six months thereafter. Applications for regulatory approval for this drug have not yet been made but the ORION-4 trial, a large-scale outcomes trial to determine whether it is beneficial for patients who have suffered acute coronary syndromes, is currently in its early stages.

Finally, moving away from the PCSK-9 pathway, bempedoic acid (ETC-1002) inhibits liver ATP-citrate lyase – the step preceding HMG-CoA reductase (the target of statin therapy). It reduces LDL-cholesterol by about 20% and adds to the effect of statins (except possibly at the highest doses). It resembles ezetimibe in its characteristics and it may find a use in combination with ezetimibe in patients intolerant of statin therapy. In February 2019, Esperion announced that they had made regulatory submissions for both bempedoic acid and a bempedoic acid/ezetimibe combination tablet.

The evolutionary cycle has turned and statins are no longer seen as the forefront of lipid therapy. New approaches are now available and only time will tell whether they succeed in the drug evolutionary challenge. BMS

Tim Reynolds is a Consultant Chemical Pathologist at University Hospitals of Derby and Burton. He will be delivering a talk at IBMS Congress 2019 on 25 September entitled "Lipid screening – current practice and evolving treatments". For more information visit **congress.ibms.org**

Left. Dr Jonathan Hartwell (right) and his assistant Sylvy R Levy Kornberg conduct some of the earliest chemotherapy tests at the National Cancer Institute, about 1950.

WAR ON CANCER PT.2

LANDMARKS IN THE DEVELOPMENT OF CHEMOTHERAPY

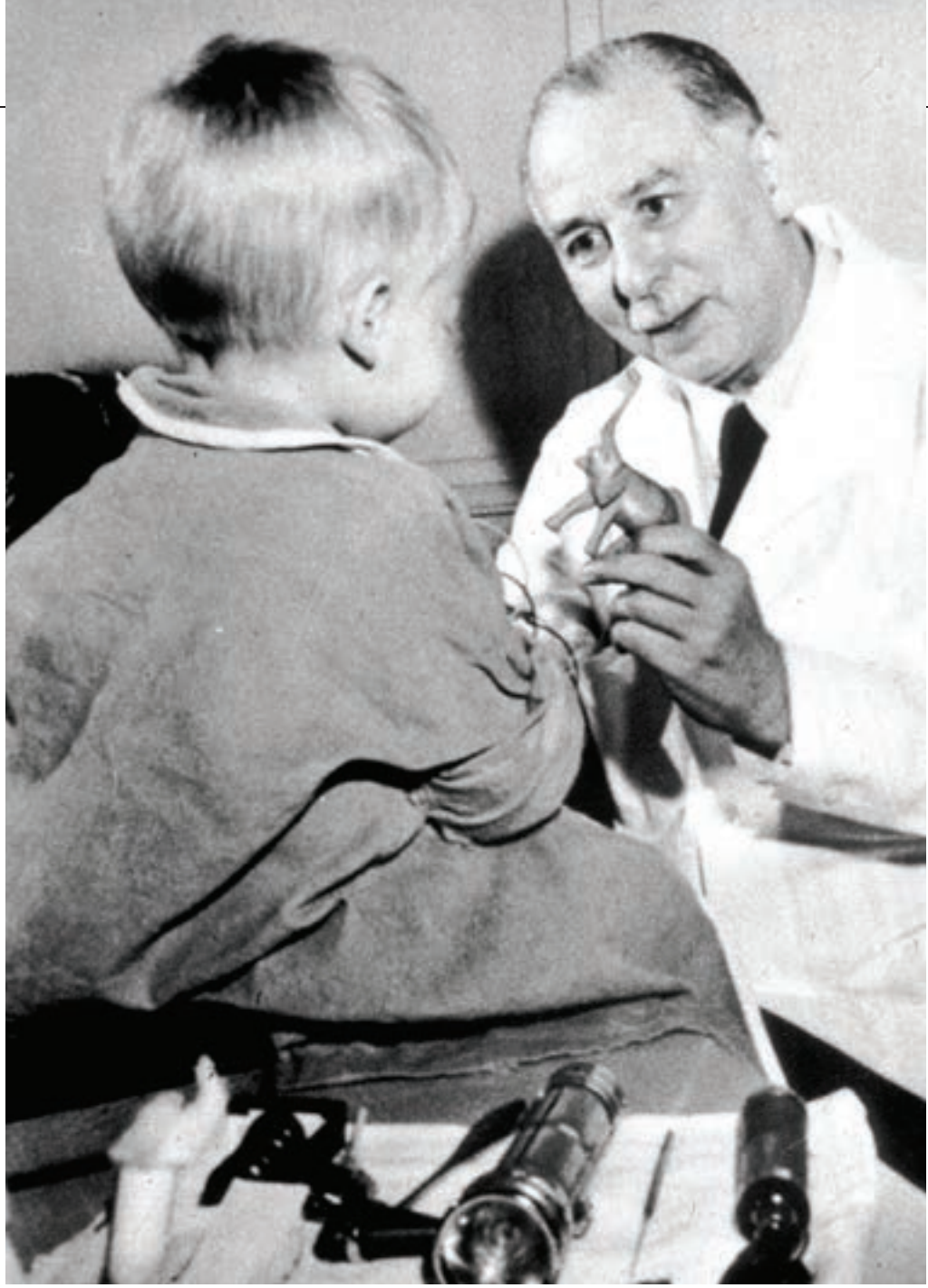
The second article of two, which briefly reviews the historical developments and use of chemotherapy since 1948 to treat different cancers.

The early years of the 1950s were a watershed in the history of chemotherapy, it would appear that cautious optimism was countered by serious, but well intended reservations on the clinical benefits of chemotherapy and quality of life issues. This was due, in part, to the transitory nature of remissions and often severe side effects of treatments. However, this was about to change dramatically with a range of clinical successes, combined with a number of significant advances in understanding the biology of the cell and genetics of cancer leading to a more structured, scientific and targeted approach to the development of more effective chemotherapeutic agents. Future cancer drugs would attempt to counter the proliferation of cancer cells targeting relevant cellular processes, notably mitosis and DNA synthesis. Surprisingly perhaps, many important agents of this period were derived from plant sources, often after long, complex and laborious experimentation and sometimes with much good fortune.

The antimetabolites

Methotrexate

In 1948, Sidney Farber showed that chemical agents antagonistic to folic acid could achieve short term clinical remission in childhood acute lymphoblastic leukaemia (ALL) with aminopterin. Other antagonists were developed and amethopterin (methotrexate) was shown to be the most effective therapeutically. Methotrexate (MTX) has a number of structural similarities to folic acid and is now known to act as a competitive inhibitor of dihydrofolate reductase, which catalyses the conversion of inactive dihydrofolate to active tetrahydrofolate, which is required for the synthesis of nucleotide bases



purines and pyrimidines, which are structural components of DNA and RNA, which regulate the synthesis of proteins to drive mitosis. In 1951, Jane C Wright, a US pioneer researcher in cancer chemotherapy at the Harlem Hospital Cancer Centre in New York, successfully used MTX in the treatment of solid tumours with remissions in breast cancer and later MTX was used in combined chemotherapy to improve effectiveness and minimise side effects. Wright and colleagues are also particularly noted for their use of tissue culture techniques to assess drugs on cultured cancer cells and improved cancer drug delivery methods. In 1958, Min Chiu Li with Roy Hertz at the National Institute, Maryland, used MTX for the effective treatment of gestational choriocarcinoma (GC) in landmark research studies.

Currently, MTX can be used alone or in combination chemotherapy for GC, ALL, breast, epidermoid cancers of head and neck, T-cell lymphoma, lung cancer and osteosarcoma. Unfortunately, side effects are common and affect normal proliferating cells, so there may be bone marrow suppression, oral, skin, gastrointestinal tract or bladder inflammation, and lung fibrosis.

Purine and pyrimidine analogues – 6 mercaptopurine & 5 fluorouracil

US biochemist George Hitchings developed a special interest in DNA bases, notably purines, at Harvard and joined the Wellcome Research Laboratory in New York in 1942 and employed young chemist, Gertrude Elion, as his assistant in 1944. This proved to be a most fruitful working collaboration in pioneering the development of a range of effective drugs and in 1948 they isolated a competitive inhibitor of adenine metabolism in *L. casei,* which interrupted cell growth and was later shown to be an immunosuppressant in rabbit studies. By 1951 numerous purine analogues had been assessed and 6 mercaptopurine (6MP) was chosen for trials using mice at the Sloan Kettering Cancer Centre, New York, and later with some success in human childhood leukaemia there and was quickly approved by the FDA in 1953 alone or combined with methotrexate. 6MP continues to be used in the chemotherapy of ALL and lymphoblastic lymphoma. Elion and the research term developed other clinically effective drugs, such as Daraprim (malaria), allopurinol (gout), azathioprine, an immunosuppressant used in organ transplants, and acyclovir for herpes infection. For these achievements, Hitchings and Elion were awarded the Nobel Prize in Physiology or Medicine in 1988, along with Sir James Black the Scottish physician and pharmacologist who developed the beta blocker propranolol and cimetidine for the treatment of peptic ulcers.

"Farber conducted a clinical trial with radiation treatment in children"

5 Fluorouracil

Working at the McCardle Laboratory at

Left. Sydney Farber

the University of Wisconsin, Charles Heidelberger and colleagues pioneered cancer research from the late 1940s. They used isotopes to study metabolic processes in cancer cells and the malignant transformation of mammalian cells in culture. They turned their attention to the development of anti-cancer drugs following a report of an increased uptake of the pyrimidine base uracil in rat hepatoma issues. They found that a fluorine substituted uracil, and 5 fluorouracil (5FU) inhibited the biochemical pathway to thymidylic acid and so interfered with DNA/RNA synthesis to limit tumour growth.

A clinical trial of purified 5FU performed in 1958 with 103 patients with a variety of solid tumours, leukaemias and lymphomas showed encouraging results and paved the way for a long-term future for 5FU alone or in combination in the treatment of cancers of breast, gastrointestinal tract and with folinic acid in advanced colorectal cancer.

Cytotoxic antibiotics

Dactinomycin

During the mid-1950s, antibiotics as growth inhibitors were considered potential candidates as anti-cancer agents. A decade earlier, a soil microflora research team led by US microbiologist Selman Waksman at Rutgers University, New Jersey USA, isolated actinomycin D from *Actinomyces antibioticus*. Actinomycin D was shown to inhibit certain transplantable tumours in mice and in 1955 Sidney Farber conducted a clinical trial of actinomycin D combined with radiation treatment in children with a variety of tumours, notably Wilms' kidney tumour. He found in many cases it prevented local recurrence and achieved clearance of metastases in the lungs with a significant improvement in their two-year survival rate. Further trials in the following two years confirmed these findings, including that led by Donald Pinkel at Roswell Park, New York. Side effects include bone marrow suppression and a risk of liver toxicity. Now known as dactinomycin, it was approved by the FDA in 1964 and is currently used in the chemotherapy of children with Wilms' tumour, rhabdomyosarcoma and in women with gestational trophoblastic disease. It is now known that dactinomycin acts by insertion into the structure of guanine and cytosine base pairs to interfere with DNA transcription at high dosage, while blocking RNA synthesis at lower doses. Other cytotoxic antibiotics used in cancer chemotherapy include bleomycin, mitomycin C and doxorubicin.

Mitotic spindle poisons

Vinca alkaloids – Vinblastine, Vincristine and Vinorelbine

During the early 1950s there was an intensive drive to investigate natural plant and marine sources for their medicinal properties including chemotherapy. In 1954 a research team led by Robert Noble at the Collip Laboratory at the University of Western Ontario, fortuitously found that extracts from the leaves of the Madagascar periwinkle plant *Vinca rosea* had a mild anti-hyperglycaemic property and, more significantly, a profound effect on the bone marrow and lowered white blood cell counts in the rats studied. In 1958 Noble with his colleague Charles Beer isolated and characterised vinblastine, a potent alkaloid extract and with the support of Eli Lilly Pharmaceuticals the first successful clinical trial of children with acute lymphoblastic leukaemia at Princess Margaret hospital in Toronto commenced in 1959. Research was continued by Eli Lilly in Indianapolis, Indiana, and in 1963 Irving Johnson led a team to perform intensive chemical and biological studies of over 30 alkaloids from *Vinca rosea*, notably vinblastine (VB) and vincristine (VC) and reviewed their activity against a wide range of cancers, notably Hodgkin's, lymphomas and leukaemias. Vinorelbine was synthesised much later during the 1980s by the late French pharmacologist Pierre Potier and has been approved for non-small cell lung cancer, and stage 4 breast cancer. Side effects include nausea, vomiting and peripheral neuropathy.

It is now known that the vinca alkaloids act as mitotic spindle poisons, binding to tubulin, unit components of the microtubules, thus inhibiting mitosis of actively dividing cells. VB has been selected for therapy in testicular cancer, Hodgkin's and non-Hodgkin's lymphoma, breast and germ cell tumours, but may cause nausea, vomiting, fever and chest pain and lower the white cell count. VC has been approved for acute leukaemia, neuroblastoma, rhabdomyosarcoma, Wilms' tumour and Hodgkin's lymphoma, but may suppress the bone marrow and cause peripheral neuropathy.

Combination chemotherapy (CC)

CC was pioneered by Emil Frei III, Emil Freireich and James Holland in 1965 for the US National Cancer Institute divisions in Maryland and Texas. Used in ALL, combining MTX, M6P, VC and prednisone, which showed improved remission rates, whereas a single agent may encounter resistance in patients and a more rapid relapse. As anti-cancer agents act on cancer cells in different ways and at different points in the cell cycle, using CC potentially increases the chance that all cancer cells will be destroyed.

It is particularly useful in solid tumours, such as lung cancer, to reduce the risk of recurrence, improve survival and response to treatment. As expected there are possible disadvantages with a danger of drug interactions and more side effects, which may be more manageable now with the use of anti-emetics and Neulasta, a cytokine, which can boost white blood cell count.

IMAGES: NATIONAL CANCER INSTITUTE

Taxoids – Taxol and Taxotere

Taxoids are a series of complex polycyclic compounds with oxygen containing functional groups derived from the bark and needles of the Pacific Yew *Taxus breviflora* or European Yew tree, *Taxus baccata*. During the pursuit of natural plant components in cancer chemotherapy, bark samples were submitted in 1962 to the Research Triangle Institute in North Carolina for investigation led by Monroe Wall and Mansukh Wani. Extracts were found to be cytotoxic and the active component Taxol was isolated and characterised by this research team in 1967. Taxol was subsequently classified as a mitotic spindle poison, binding to cellular microtubules preventing cell division in rapidly dividing cells. Clinical trials of patients with ovarian and breast cancer were conducted at a number of US specialist cancer centres and Taxol therapy found to significantly reduce tumour size. However, there were serious side effects with severe allergic reactions and one fatality. Working with Bristol Myers Squibb Pharmaceuticals in 1991, it was renamed paclitaxel, but with limited stocks and for sound ecological reasons active research by over 30 groups were undertaken in order to synthesise Taxol. In 1994 total synthesis was achieved at the Scripps Research Institute in California by a team led by KC Nicolaou. Alternatively taxotere, a semi-synthetic derivative of taxol, was prepared by a French research team in 1992 and given the commercial name Docetaxel and later found to be active against a wide range of cancer tumours, including breast, prostate, stomach, head and neck, and non-small cell lung cancer. NICE currently recommends its use with adjuvant treatment of breast cancer and in combination regimes for other cancers, or those resistant to previous chemotherapy. NICE recommends conditional use of paclitaxel for ovarian, breast, pancreatic and non-small cell lung cancer in combination, resistant or appropriate chemotherapy.

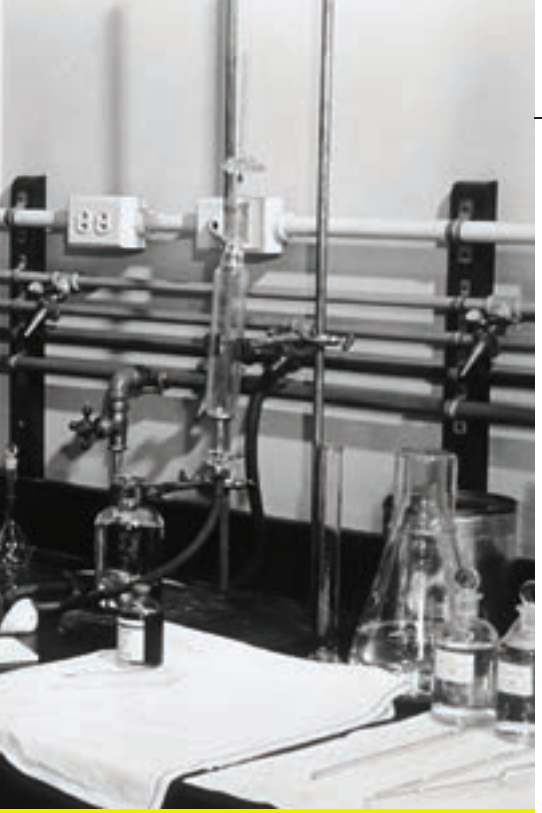
Topoisomerase inhibitors – camptothecin, irinotecan, etoposide

Topoisomerases (TIM 1 and 2)

TIM 1 was first described in 1971 by James Wang, a Chinese born US biochemist and shown to alter the 3D structure of DNA by separation, unwinding and recombination reactions during replication and transcription, which limit cell mitosis. TIM 1 catalyses these actions in single-stranded DNA, while TIM 2 acts on double-stranded DNA. Camptothecin (CPT) was another anti-cancer agent discovered by Wall and Wani in 1966 at the Research Triangle Institute from the bark and stem of a Chinese ornamental tree, *Camptotheca acuminate* (Happy tree) and was found to be a potent anti-tumour agent in early clinical trials in 1988, and acts by binding to TIM 1-DNA preventing DNA replication. But as for Taxol, difficulties were encountered, due to its low solubility but also there were serious risks to renal function. As a consequence, research groups investigated synthesis procedures for CPT and analogues but it was not until 1996 when a suitable and stable analogue, irinotecan, was prepared. With the collaboration of the Christus Stenlin Foundation, another analogue 9 NitroCPT was developed with low toxicity and used in a clinical trial in patients with advanced pancreatic cancer and showed a modest improvement in survival time. Irinotecan has been used to treat colon cancer and small cell lung cancer in combination with fluorouracil and cisplatin, respectively. And is also recommended in the treatment of metastatic adenocarcinoma of the pancreas. The most severe side effects are diarrhoea and suppression of the immune system.

EXAMPLES OF COMBINATION CHEMOTHERAPY

Combination	Cancer types
5 Fluorouracil/Methotrexate	Colorectal cancer
Cyclophosphamide/5 Fluorouracil/Methotrexate	Breast cancer
Cisplatin/Vinorelbine	Small cell lung cancer
Doxorubicin/Bleomycin/Vinblastine/Dacarbazine	Hodgkin's lymphoma
Doxorubicin/Cyclophosphamide	Breast cancer
Bleomycin/Etoposide/Cisplatin	Testicular cancer
Cyclophosphamide/Doxorubicin/Vincristine	Small cell lung cancer
Cyclophosphamide/Doxorubicin/Vincristine/Prednisone	Non-Hodgkin's lymphoma
Cisplatin/5 Fluorouracil	Oesophageal & Head and Neck
5 Fluorouracil/Folinic acid/Oxaliplatin/Taxotere	Oesophageal, Gastric
Irinotecan/5 Fluorouracil/Folinic acid	Colorectal cancer
Melphalan/Predisone/Thalidomide	Myeloma
Taxol/Ifosfamide/Cisplatin	Testicular & Germ cell cancers
Carboplatin/Vincristine/Etoposide	Retinoblastoma
5 Fluorouracil/Methotrexate/Doxorubicin	Gastric
5 Fluorouracil/ Folinic acid	Colorectal cancer



Left. Howard Skipper, from Southern Research Institute in Birmingham, Alabama

HOWARD EARLE SKIPPER (1915–2006)

Howard Skipper was a US oncologist who, after qualification at the University of Florida, served in the US Army Chemical Warfare Service 1941-45 and gained some experience in anti-cancer agents with nitrogen mustard. In 1946, he joined the Southern Research Institute, Birmingham, Alabama and with chemists Lee Bennett Jr, John Montgomery and virologist Frank Schabel, established a dynamic cancer research programme. The main focus was to develop quantitative animal models to screen potential anti-cancer drugs, notably for the treatment of leukaemia and lymphomas, using murine leukaemia cell lines. The team also studied the kinetics of tumour growth and developed protocols for monotherapy and combination chemotherapy in seminal experiments during the 1960s, which were crucial to the preclinical testing of numerous agents. High dose chemotherapy was advocated by this group. The early screening *in vivo* models were L1210 and P388 murine leukaemia, used in 1955-1975 with some success for identifying agents for the treatment of leukaemia and lymphoma. Today the US National Cancer Institute holds a bank of over 60 human cancer cell lines.

"Skipper gained some experience in anti-cancer agents with nitrogen mustard"

Etoposide (EP)

There is evidence that extracts from *Podophyllum* plants have an ancient history as medicinal plants as recorded, by Dioscorides, a Greek physician and pharmacologist. Investigations began in the early 1950s to explore this potential using extracts of the rhizome of *Podophyllum peltatum* (American mandrake) at the Sandoz laboratories in Basel, Switzerland. Over two decades of research by a team led by Hartmann Stahelin and Albert von Wartberg was required to prepare the semi-synthetic derivative etoposide which showed cytotoxic potency and prolonged survival on the L1210 leukaemic mouse model in 1966, and clinical trials were conducted in 1971. However, it would be a further 12 years for FDA approval. There were intensive studies on the mechanism by which etoposide acts and studies by Minocha and Long in 1983 showed that etoposide inhibits TIM 2 by binding to DNA to cause strand breakage and inhibit DNA replication. Etoposide has been used in chemotherapy, often in combination for testicular cancer, ovarian cancer, lung cancer, leukaemias and neuroblastoma. Side effects include bone marrow suppression, allergic reactions and increased risk of infection.

Platinum compounds – cisplatin and carboplatin

First investigated by Barnett Rosenberg, a biophysics researcher, in 1965 at Michigan State University, who observed that cell division of *E. coli* ceased during electrolysis using platinum electrodes. Further work performed identified a soluble cytotoxic compound released from the platinum electrodes as cisplatin and found positive results with a sarcoma mouse model but nephrotoxicity at high doses. Clinical trials began in 1972 at Indiana University led by Lawrence Einhorn with highly successful results using combination chemotherapy with cisplatin, vinblastine and bleomycin in patients with metastatic testicular cancer. FDA approval was achieved in 1978 and also for patients with ovarian and bladder cancer. Analogues, notably carboplatin, were developed later by a research team at the Institute of Cancer Research in London, UK and reported in 1983 showing less toxic side effects. Carboplatin can be used in ovarian, lung and head and neck cancers but is less effective than cisplatin in certain testicular cancers. Cisplatin has also been used alone, or in combination, for cervical cancer and certain brain tumours, but side effects may be common and are often serious.

Concluding comments

This has been a fascinating period for chemotherapy with a range of approaches adopted to destroy cancer cells, and the use of natural plant sources to derive anti-cancer agents, synthesise analogues, and collaboration with pharmaceutical companies. The trials and tribulations of cancer drug development is well exemplified by Taxol and etoposide and likewise good fortune in the discovery of vinblastine and cisplatin.

It is the initiative, dedication and scientific quality of the research scientists and oncologists included in this short review which is so impressive. Innumerable people have made invaluable contributions in the war on cancer, which nevertheless continues. IBMS

Stephen Clarke is a retired IBMS Fellow.
To see the references, view the article online at **thebiomedicalscientist.net**

BIOMEDICAL SCIENCE DAY 2019

This year Biomedical Science Day will be held on **Thursday 20 June**. Once again, we want our members to celebrate their work in biomedical science and show patients, hospital staff and the public the vital role they play in healthcare. Free with this month's edition of *The Biomedical Scientist* you'll find a poster to put up at work to help encourage colleagues to take part.

Fun and interactive stands

Nothing says Biomedical Science Day like a fun and interactive stand. We love to see displays in reception areas and lobbies – where the hospital's largest footfall can engage with biomedical science activities, information and freebies.

A charity bake sale is a great way to attract people, as are activities involving science and microscopes. We also have three new sample journey videos at samplejourney.com. They are great for catching the eye and drawing people towards your stand – but you will need a screen. Do you know who looks after your video displays?

The overall key to running a stand while maintaining excellent service delivery is usually cross-department co-operation. One person can take the lead but, if you are that person, reach out and see if you have a team of people willing to help you keep the stand running all day.

Laboratory tours

Laboratory tours are the most immediate and effective way to inform people about the profession. Everybody loves to see what happens behind the scenes – not to mention that they can empower patients and strengthen interdisciplinary team work and communication. However, there are health and safety issues surrounding certain laboratory practices and spatial issues in some laboratory set-ups. Before you commit to giving tours, talk to your laboratory manager and make sure they are practical in your department.

If you want to advertise your laboratory tours internally, we have an A3 poster you can print and put your details on. Download it at ibms.org/public-engagement.

Resources and freebies

Members can order our Biomedical Science Day event packs, which include posters, leaflets, placards, fluffy bugs, stickers and badges. To order your box, please complete the online application form located in the resources section of our Biomedical Science Day website – biomedicalscienceday.com.

To ensure we can complete all orders in time, requests for Biomedical Science Day goodies must be received by Thursday, 6 June.

We are also excited to have launched our *Superlab* activity magazine for children aged 7–11, helping them to learn that scientists work in hospitals and are a big part of healthcare services. For Biomedical Science Day, you'll receive some with your box of promotional materials so that you can give them out to any children who come to your stands or on your laboratory tours. If you plan to visit primary schools to promote biomedical science, then you can order more from us via ibms.org/public-engagement.

Unique stories

Hosting tours and exhibiting on stands are great for raising awareness on a local level, but to reach wider audiences you need a story. We have standardised press releases and social media posts available in the resources section of our website, so that you can publicise your events to local media and your social media followers. However, to gain the interest of national media, you will need an angle. Perhaps you are making the switch to digital and can showcase the future of the NHS. Maybe changes to your laboratory have had a positive impact on patients with a diagnosis that gains media attention. Perhaps you have a connection who can draw a crowd. The presence of an MP or a celebrity often draws extra attention to a press release.

Think about whether your department can tell a Biomedical Science Day story. If you've got something in mind, contact us and we will help you get your message out to the right people. Email communications@ibms.org

Communications

Hospitals and trusts have communications teams and they should be informed of your Biomedical Science Day plans, as they can help you attract the press and public into your hospital.

You should also talk to them about taking over their social media accounts on Biomedical Science Day to promote your work and events.

We are also happy to collaborate with communications teams, if they want to talk to us – communications@ibms.org. It's also worth remembering that our members can wear their "IBMS hats" in any public relations where they are promoting the profession and don't have to be speaking on behalf of their hospital.

Activity fund

If you are planning to organise a big event for Biomedical Science Day, consider applying for the Biomedical Science Day Activity Fund. The fund provides grants of up to £500 for IBMS members to develop their biomedical science related activities and events. Please complete our online application form (biomedicalscienceday.com) by Friday, 17 May.

Most importantly…

Have fun! Go out there and show people what a wonderful profession you are a part of! BMS

COMPETITIONS

Show the world how your work is #AtTheHeartOfHealthcare

This year, we have some fantastic awards and prizes on offer for our photo competitions. Help us raise awareness of the vital role of biomedical science in healthcare by sending us your photos. Prizes and awards this year will be for:

1. **Best Biomedical Science Day display**
2. **Best group photo with placard**
3. **Best individual photo with placard**
4. **Best group workplace photo**
5. **Best individual workplace photo**
6. **Best biomedical bake (best cake)**
7. **Best artistic photo**
8. **Best biomedical science video**
9. **Best biomedical science photo**
10. **Best biomedical science meme**

To enter, simply submit your photos to us on Biomedical Science Day via our Facebook page (@biomedicalscience), tweet your picture to us (@IBMScience) using #AtTheHeartOfHealthcare or send it via email to website@ibms.org and we'll add it to our online gallery.

Please note: Always make sure there are no confidential details visible, maintain workplace health and safety regulations and ensure you have permission to take photos, from both your senior management and anyone appearing in them. The IBMS may use images you submit for marketing purposes, including on our social media channels or website. By sending us your photo you are consenting to us using it.

HOW TO... EMBRACE LEADERSHIP

Clinical Scientist and Molecular Pathology Lead **Siobhan Taylor** discusses applying for a leadership programme and the benefits it has brought.

The last 12 months have been a personal journey of self-discovery and realisation. It was while attending the Women in Healthcare Science Leadership day in May 2018 that I realised how intrinsically linked my future career goals were to the development of my leadership abilities. I was inspired to hear from other female healthcare scientists and network with like-minded, ambitious female healthcare scientists from across the sector.

In January 2018, I was the only Clinical Scientist working within a large histology laboratory in Cheltenham. My role is unique and largely based around the development and management of the HER2 and molecular pathology services. I have always been committed to my own personal development and passionate about providing a patient-focused, effective and efficient service, but I was struggling to recognise my capabilities and this was impacting future progression.

I was looking into the Higher Specialist Scientific Training programme (HSST) and a colleague put me in touch with Dr Jo Horne, a dual registered scientist also working in histology, and an existing CSO WISE Fellow. During our communications, Jo suggested I seriously consider applying for the 2018 Fellowship.

First steps

I recalled seeing the advert in March encouraging "aspiring female leaders to apply for this highly prestigious and competitive programme". I was excited. It sounded like an excellent opportunity and I fitted the eligibility criteria. But this was quickly followed by thoughts of self-doubt: I will never make it through the application process. What have I got to offer? How is leadership relevant to my career goals? And how would I fit it around my existing responsibilities of part-time working and mother to two young children? Jo's encouragement thankfully made me re-consider.

The application process itself was a rewarding and valuable self-reflection exercise, helping me to appreciate just how much I have achieved in my career, and how much leadership has been pivotal in that journey.

The Career Development Programme (Skills 4 UK) in the early part of the Fellowship consisted of four one-day workshops addressing communication styles and effective communication, presentation skills and goal setting. It has given me a greater self-awareness with an overall effect of improved self-confidence. I have always shied away from seeking feedback, but with a new-found strength and courage, I have learnt how valuable it can be in identifying areas of development. From this new-found understanding, I have come to believe in my own ability, tap into my strengths and know how to build and focus on becoming the best I can be.

I feel equipped with the tools to embrace and better deal with the outcomes of challenging situations, and more confident communicating at all levels of the organisation, allowing me to influence effectively. I have been able to bring this learning back to my own team, supporting and encouraging colleagues in their own development. I have also led in the innovation of my areas, taking on new responsibilities and developing services allowing me to have a greater impact on my department, my trust and overall patient care. Whilst the mentoring element of the Fellowship is still in the early stages, it is already allowing me to break down my goals into smaller actions

and take my ideas to a higher level, bringing them to life at accelerated speed.

Working together

The three Fellows with whom I joined the programme have been a source of inspiration and support to me, acting as a soundboard and offering practical advice when I have needed it. I think it fair to say that all four of us have come to appreciate how intertwined our roles are within the patient care pathway, all working to achieve the same outcome. I have come to appreciate the value of a network that reaches beyond my own team, my own trust and my own discipline of HCS. I have had the fortune of attending the CSO conference and a number of NHS England Healthcare Science meetings, as well as *The Lancet* "Advancing women in science, medicine, and global health" London launch in February this year. These, in combination with getting in touch with my lead healthcare scientist, have really highlighted the importance of all healthcare scientists working together, to raise our profile and allow us to contribute more effectively to the delivery of the *NHS Long Term Plan*.

I have long wanted to use my experiences to inspire future generations with school outreach and this year I took the plunge, finding it a rewarding and valuable experience. Both the mentoring aspect of the Fellowship, and involvement with WISE has highlighted the importance of role models, particularly for women in STEM; I am excited to start running their outreach programme "My Skills My Life" in local schools as soon as I have completed training.

The last year has intensified my desire to be the best that I can be and I am excited and optimistic for what the remainder of my career could be, with a little carefully planning, a new-found confidence and the right support network. So, what advice would I give to anyone reading this and considering the opportunity? If you want to explore who you are and what kind of leader you could be – be brave, push aside the self-doubt and apply. Find out who your trust lead healthcare scientist is and get in touch. Join twitter and expand your network. This year, the amended CSO WISE Programme is being offered to 32 applicants, it's an opportunity to realise your own potential, increase your contribution and impact on patient care and inspire future generations. The benefits are far reaching – you have nothing to lose and everything to gain. BMS

Siobhan Taylor is the current recipient of the Chief Scientific Officer Women in Science and Engineering Fellowship.

Follow Siobhan on twitter at siobhanT1979. The CSO WISE Healthcare Science Leadership Development Programme for NHS England is now talking applications for 2019. The deadline to apply is 10 May. For application details and further information on WISE, visit wisecampaign.org.uk

"I have come to appreciate the value of a network that reaches beyond my own team, my own trust and my own discipline"

MY IBMS NEWS

ADVANCING HEALTHCARE AWARDS

SCIENTISTS SCOOP ACCOLADES

IBMS members were victorious at the Advancing Healthcare Awards (AHAwards) for achievements in biomedical science.

The AHAwards recognise the achievements of allied health professionals, healthcare scientists and support staff. Among the winners were IBMS Fellow Dr Jo Horne and IBMS Licentiates Danny Gaskin and Chloe Lockwood, while IBMS members were among those shortlisted. IBMS Fellow Dr Mary Hannon-Fletcher received a special recognition award for her 40-year career in biomedical science.

The awards included IBMS Biomedical Scientist of the Year – the second year the IBMS has sponsored an AHAward. The award celebrates an exceptional biomedical scientist who uses their skills and expertise to advance practice in an innovative and impactful way, making a real difference to patients' lives and inspiring those around them.

Award winners and shortlisted finalists

The College of Podiatry Rising Stars award

Danny Gaskin, Milton Keynes University Hospital - **winner**

Chloe Lockwood, St James University Hospital - **winner**

The Biomedical Scientist of the Year award

Sarah Brownsteen, Gloucestershire Hospitals NHS Foundation Trust - **shortlisted**

Jo Horne, Southampton General Hospital - **winner**

Shauna McAuley, Royal Victoria Hospital - **shortlisted**

Special recognition award

Dr Mary Hannon-Fletcher

The AHCS award for Inspiring the healthcare science workforce of the future

Bamidele Farinre, Great Ormond Street Hospital - **shortlisted**

The Scottish Government Award for driving improvement, delivering results

Sarah Smith, Lynne Taylor, Claire Cameron - **winner**

Dr Mary Hannon-Fletcher has trained biomedical science staff in the UK and overseas, both in the laboratory and as an academic at Ulster University. Upon receiving her special recognition award she said: "Receiving this recognition for my work over the years championing biomedical science both clinically and as an academic, educating and training biomedical scientists, ensuring they are leaders in the future of healthcare, means so much to me as it is awarded by my peers. The event was so encouraging; seeing so many dedicated colleagues going above and beyond for their clients and then receiving recognition for their work was heart-warming."

IBMS President Alison Geddis presented Mary with her award and commented: "Mary has encouraged innovation and research within biomedical science throughout her long career. She champions and raises the profile of biomedical scientists at every opportunity, and truly deserves this special recognition award."

Dr Jo Horne was nominated for the IBMS Biomedical Scientist of the Year award for her work promoting biomedical science and as a pioneer and role model in the delivery of histopathological reporting.

Annual General Meeting programme

8 June 2019

12 Coldbath Square, London

Registration and coffee:
9.30 – 10.00

Presentation:
10.00 – 11.00

'A day in the life of death' by Daisy Shale MSc CSci FIBMS, Senior Medical Examiner's Officer, Sheffield Office

The loss of a close relative is a particularly difficult time for families, and at such a time they need to have confidence in the public services associated with the certification of death and burial or cremation. For most families their experience of the process surrounding the death of a family member is satisfactory,at least given the circumstances,b ut there is a possibility of things going wrong. The Harold Shipman case highlighted the thankfully rare but potentially devastating effects of criminal activity relating to death certification,but subsequent events in Mid Staffordshire, Southern Health,an d others have highlighted the importance for an independent review of events,car e and cause of death, to ensure any concerns with care are raised, addressed and learnt from. From April 2009 the Department of Health and Social Care has been working towards developing a system where every death,that does not undergo coroner investigation,is r eviewed by an independent doctor known as a medical examiner. April 2019 saw the phased roll out of a national system to provide much-needed support for bereaved families and to improve patient safety.

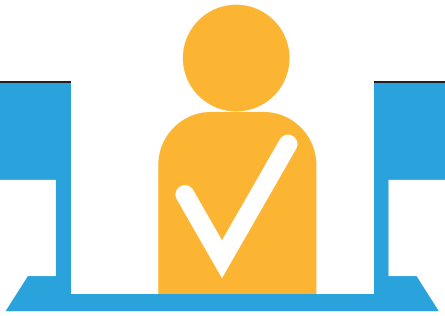
Registration for the Annual General Meeting
11.00 – 11.30

Annual General Meeting and Awards
11.30 - 12.30

Lunch
12.30 – 13.30

Close
13.30

Should you wish to attend the morning lecture and the AGM, please email the office at AGM@ibms.org by noon on Friday 17th May



ANNUAL GENERAL MEETING 2019

NOTICE IS HEREBY GIVEN that the seventy-seventh annual general meeting of the Institute of Biomedical Science (Institute) will be held at the Institute of Biomedical Science, 12 Coldbath Square, London EC1R 5HL on Saturday 8th June 2019 at 11.30 am to:

1. **Receive the annual members' report of the Institute for 2018 and accounts for the fifteen months ended 31 December 2018, together with the report of the auditors**
2. **Appoint the auditors for the ensuing year**
3. **Announce the result of the elections for national and regional members of Council**
4. **Consider and, if thought fit, to pass the following special resolution proposed by the Council:**

Special Resolution Proposed By The Council

To amend the Articles of Association of the Institute by making the following addition to Article 16:

Current text:

"A member shall cease so to be if the Council considers him to have been guilty of improper conduct rendering him unfit to be a member of the Institute. Upon the Council receiving notice of any event which has rendered a member liable to have his name removed the register such member shall be given notice thereof and invited to attend or be represented before the council and to make such explanation as he may think fit."

Revised text, with added sentence highlighted in bold

"A member shall cease so to be if the Council considers him to have been guilty of improper conduct rendering him unfit to be a member of the Institute. Upon the Council receiving notice of any event which has rendered a member liable to have his name removed from the register such member shall be given notice thereof and invited to attend or be represented before the Council and to make such explanation as he may think fit, **provided that if the member in question has been struck off a statutory register the membership of such member shall automatically terminate without the right to be heard before the Council."**

12 Coldbath Square
London EC1R 5HL
1st May 2019

By order of the Council
Jill Rodney
Chief Executive and Company Secretary

VOTING BY PROXY

1. A member entitled to attend and vote at the above meeting may appoint a proxy to attend and on a poll to vote instead of him/her. Any proxy so appointed must be a member of the Institute.
2. The instrument appointing a proxy shall be deposited at the registered office of the Institute not less than 48 hours before the time for holding the meeting or adjourned meeting at which the person named in the instrument proposes to vote.
3. An instrument appointing a proxy shall be in writing, executed by the appointer, and shall be in the form prescribed in Article 43 of the Institute's Articles of Association.
4. The instrument appointing a proxy shall be deemed to confer authority to demand, or join in demanding, a poll.

Proxy Institute of Biomedical Science

I ..... of .....
being a member of the Institute of Biomedical Science, and entitled to vote, hereby appoint as my proxy

..... of ..... a member of the Institute, or failing him the duly appointed chairman, to vote in my name and on my behalf at the annual or extraordinary general meeting of the Institute of Biomedical Science to be held on the 8th day of June 2019 or any adjournment thereof. In the absence of any conflicting instructions the proxy may vote as he thinks fit or abstain from voting.
I instruct my proxy to vote as follows (Circle the desired option)

Resolution Article 16: to amend the Articles of Association of the Institute in the manner put forward in the draft resolution **For/Against/Discretion**

Dated this day of .....

Signed .....

The instrument appointing a proxy shall be deemed to confer authority to demand or join in demanding a poll.

JOURNAL-BASED LEARNING EXERCISES

Please select your choice of correct answers and complete the exercises online at: **www.ibms.org/cpd/jbl**

DEADLINE WEDNESDAY 7 AUGUST 2019

Early colposcopic reassurance and discharge to routine recall does not increase subsequent high-grade referral or treatment rates.

Macdonald M, Lyon R, Smith J, Tidy J, Palmer J. *Cytopathology* 2017; **28** (5): 407–12. Assessment No: 050819

01	Referrals for moderate dyskaryosis or worse increased by 19% between 1 April 2014 and 31 March 2015.
02	Each year since 1 April 2011 there has been a significant increase in the number of referrals with high-grade cytology to the Jessop Wing colposcopy unit.
03	Treatment rates increased by 49% since 2011.
04	The study data were gathered from pathology and colposcopy databases and cross-referenced with women referred with high-grade dyskaryosis and those who had undergone LLETZ treatment.
05	Cytology specimens were processed using ThinPrep, and HPV tested using cobas 4800.
06	1765 women underwent LLETZ treatment with a median referral age of 39.
07	96% of women referred had an abnormal cervical screening sample.
08	12% of women in the 'see and treat' group had no CIN in their LLETZ specimen.
09	There was a significantly higher likelihood of a negative LLETZ in the women previously discharged to routine recall as compared with those not previously seen in colposcopy.
10	In the women previously discharged to routine recall from colposcopy there were 48 cases of CIN 3.
11	In 2014,54% of referrals resulted in a 'see and treat' procedure compared to only 39% in 2012.
12	During the study period,39 cases of invasive disease were found,none of which were in the previously seen discharged to routine recall cohort.
13	Colposcopy is highly sensitive in detecting high-grade CIN in low-grade cytology referral cases.
14	All high-grade abnormalities stain white on application of acetic acid.
15	It is suggested that biopsy may have missed an area of CIN for some of the previously seen women.
16	Some studies suggest multiple random biopsies from each cervical quadrant or area of the aceto-white change should be taken to assess women referred with low-grade cytology HR- HPV positive.
17	The study reviewed reported concordance in 50% of the punch biopsy specimens and subsequent excisional specimens.
18	Punch biopsy may act as a treatment for small high-grade lesions.
19	Pooled data from four large European trials suggest HR-HPV screening gave a 60-70% greater protection from the cervical cancer than cytology screening alone.
20	The increase seen in treatments during the study period is likely due to the increased sensitivity of HPV triage in detecting women with high-grade disease.

Laboratory assay measurement of modified clotting factor concentrates: a review of the literature and recommendations for practice.

Young GA, Perry DA. *J Thromb Haemost* 2019; **17** (4): 567–73. doi: 10.1111/jth.14394. Assessment No 050419

01	Plasmatic APTT reagents underestimate rFVIII as levels drop to 0.2 IU/mL and 0.05 IU/mL.
02	Recombinant FIX products carry no risk of transmitting human immunodeficiency virus.
03	The authors of the paper concur with the manufacturer of the FVIII-SC molecule that one-stage clotting assays can safely be used to assay FVIII-SC as long as the result is multiplied by a factor of two.
04	According to the authors,most coagulation laboratories will use only one APTT activator for all APTT-based assays.
05	According to the authors,it is the variation in the types of silica and polyphenolic acid used in commercial APTT reagents that exert different effects on the results of factor assays for the FVIII and FIX concentrates that are the subject of the review.
06	Both currently available chromogenic FIX assays correctly measure rFIX Fc.
07	The authors consider it is unlikely that each haemophilia treatment centre will be able to be fully self-sufficient in having the necessary assays available in the new era of clotting factor concentrates.
08	Haemophilic arthropathy results in only temporary joint damage.
09	Chromogenic FIX assays are not licenced in the USA.
10	Very significant over-estimation of FIX levels occurs when certain silica APTT reagents are used to assay N9-GP
11	The authors of the article indicate that the chromogenic assay can be recommended to measure recoveries of all five of the novel FVIII concentrates.
12	The source of phospholipid in APTT reagents has not been proven to impact factor assay results when used to measure the clotting factor concentrates listed in the review.
13	The chromogenic FIX assay uses excess FVIII such that the amount of FVIII in the patients plasma is irrelevant to the assay.
14	Under estimation of FVIII/FIX levels can result in under-dosing of clotting factor concentrate and put patients at risk of bleeding.
15	According to the study by Gu *et al.* (2014)correct results are obtained with SynthaSIL and Actin FS APTT reagents when used to assay N8-GP.
16	The title of citation 6 in the reference list indicates it is a comparative field study evaluating the activity of recombinant FVIII Fc fusion protein in plasma samples.
17	One-stage clotting assays using Actin FS L and CK Prest APTT reagents overestimate levels of N9-GP
18	One-stage clotting assays using CK Prest and Cephascreen APTT reagents correctly estimate levels of rFVIII Fc and N8-GP,but underestimate levels of rFVIII-SC.
19	Not all silica APTT reagents have been tested for use in one-stage clotting assays to measure rFIX Fc and rFIX P
20	One-stage clotting assays using Trinclot HS and Actin FS L APTT reagents correctly estimate levels of rFIX Fc.

REFLECTIVE LEARNING

01	The study data showed a significant increase in both the number of women referred with high-grade dyskaryosis and those undergoing treatment. Compare these findings to those seen in your own laboratory and colposcopy unit(s)for the same time period and discuss similarities and differences.
02	Given that there was a significantly higher likelihood of a negative LLETZ in women previously discharged to routine recall as compared to those not previously seen in colposcopy,could this suggest that this cohort of women is potentially being over-treated?If so,what could be the consequences?
01	Discuss the implications of limited factor assay repertoires in coagulation laboratories with respect to haemophilia treatment and monitoring.
02	Check the title of reference number 6 on the internet and discuss whether transcription errors in publications like this should be a concern.

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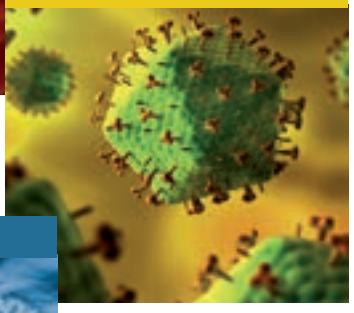
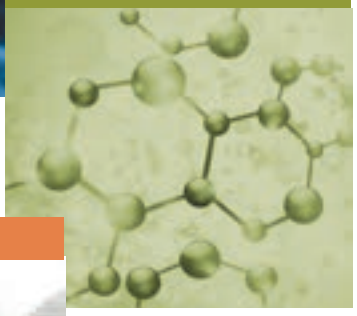


Allergology

Antigen Detection



Automation

Molecular Diagnostics

020 8540 7058
itc@euroimmun.co.uk
www.euroimmun.co.uk

IBMS Institute of Biomedical Science Continuing Professional Development

EVENTS AND TRAINING COURSES

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.

DATE	TITLE	VENUE CONTACT
May		
2 May	**One-Day Update in Cervical Cytology**	Bristol I SWRCTC@nbt.nhs.uk
2-3 May	**Focus 2019**	Glasgow I focus2019@acb.org.uk
4 May	**BDIAP Molecular Pathology Study Day**	London I lisa.browning@ouh.nhs.uk
8 May	**UK NEQAS Cellular Pathology Technique non-gynae cytology beginners/refresher workshop**	Gateshead I chantell.hodgson@nhs.net
9 May	**Achieving Excellence in Compliance and Monitoring Data Insights**	Coventry I sallycox@tutelamedical.com
9 May	**UK NEQAS Cellular Pathology Technique non-gynae cytology intermediate workshop**	Gateshead I chantell.hodgson@nhs.net
10 May	**Blood Sciences short course**	London I c.ferrier@westminster.ac.uk
14 May	**CM-PATH Biobanking Workshop – "Do we really need another Biobank?"**	London I helen.pitman@ncri.org.uk
15 May	**Association of Biomedical Andrologists Annual Conference**	Cardiff I lesley.walsh@wwl.nhs.uk
16 May	**Respiratory Microbiology – A Day of Inspiration**	London I swallis@mastgrp.com
17 May	**Blood Sciences short course**	London I c.ferrier@westminster.ac.uk
24 May	**Haematinics and white blood cell disorders**	London I c.ferrier@westminster.ac.uk
June		
5-6 Jun	**Clinical and Laboratory Haemostasis 2019; UK NEQAS for Blood Coagulation Annual Scientific Meeting**	Sheffield I tim.woods@sth.nhs.uk
6 Jun	**IBMS Registration Portfolio Workshop**	London I c.ferrier@westminster.ac.uk
6 Jun	**Update in Cervical Cytology for pathologists, consultant BMS and holders of the Advanced Specialist Diploma in Cytology**	Bristol I SWRCTC@nbt.nhs.uk
10 Jun-21 Jul	**Introductory Course in Cervical Cytology**	Bristol I SWRCTC@nbt.nhs.uk
11-12 Jun	**Practical and Clinical Microbiology of Anaerobes**	Cardiff I deborah_robinson@dwscientific.co.uk
12 Jun	**UK NEQAS Cellular Pathology Technique TEM workshop**	Leicester I chantell.hodgson@nhs.net
13 Jun	**Quality, Audit and Improvement workshop**	Croydon I sue.alexander@rmh.nhs.uk
13 Jun	**UK NEQAS Immunology, Immunochemistry & Allergy Quality Assurance Masterclass 19**	Sheffield I ukneqas@immqas.org.uk
13-14 Jun	**Anaerobe 2019: Changing perceptions of anaerobic bacteria; from pathogen to the normal microbiota and back; a Microbiology Society-focused meeting**	Cardiff I s.gavrila@microbiologysociety.org
14 Jun	**UK NEQAS Immunology, Immunochemistry & Allergy Annual Participants Meeting EQA 2019: Maximising Quality for Patient Care 19**	Sheffield I ukneqas@immqas.org.uk
19 Jun	**UK NEQAS Cellular Pathology Technique special staining beginners/refresher workshop**	Newcastle upon Tyne I chantell.hodgson@nhs.net
20 Jun-20 Jul	**UK NEQAS Cellular Pathology Technique specialist workshop A**	Newcastle upon Tyne I chantell.hodgson@nhs.net
25 Jun	**One-Day Update in Cervical Cytology – metaplasia/cancer audit day**	Bristol I SWRCTC@nbt.nhs.uk

HERE TO HELP

HCPC STANDARDS OF EDUCATION AND TRAINING

Alan Wainwright, IBMS Executive Head of Education, summarises revisions that are due to be implemented following an audit.

The Health and Care Professions Council (HCPC) has Standards of Education and Training (SETs) against which they approve programmes and make sure that a learner who completes the programmes meets the standards of proficiency for their profession, thereby becoming eligible to apply for HCPC registration.

The IBMS provides five HCPC-approved education routes towards registration of biomedical scientists and clinical scientists with the HCPC (more information can be found on the website: ibms.org/registration/hcpc-registration).

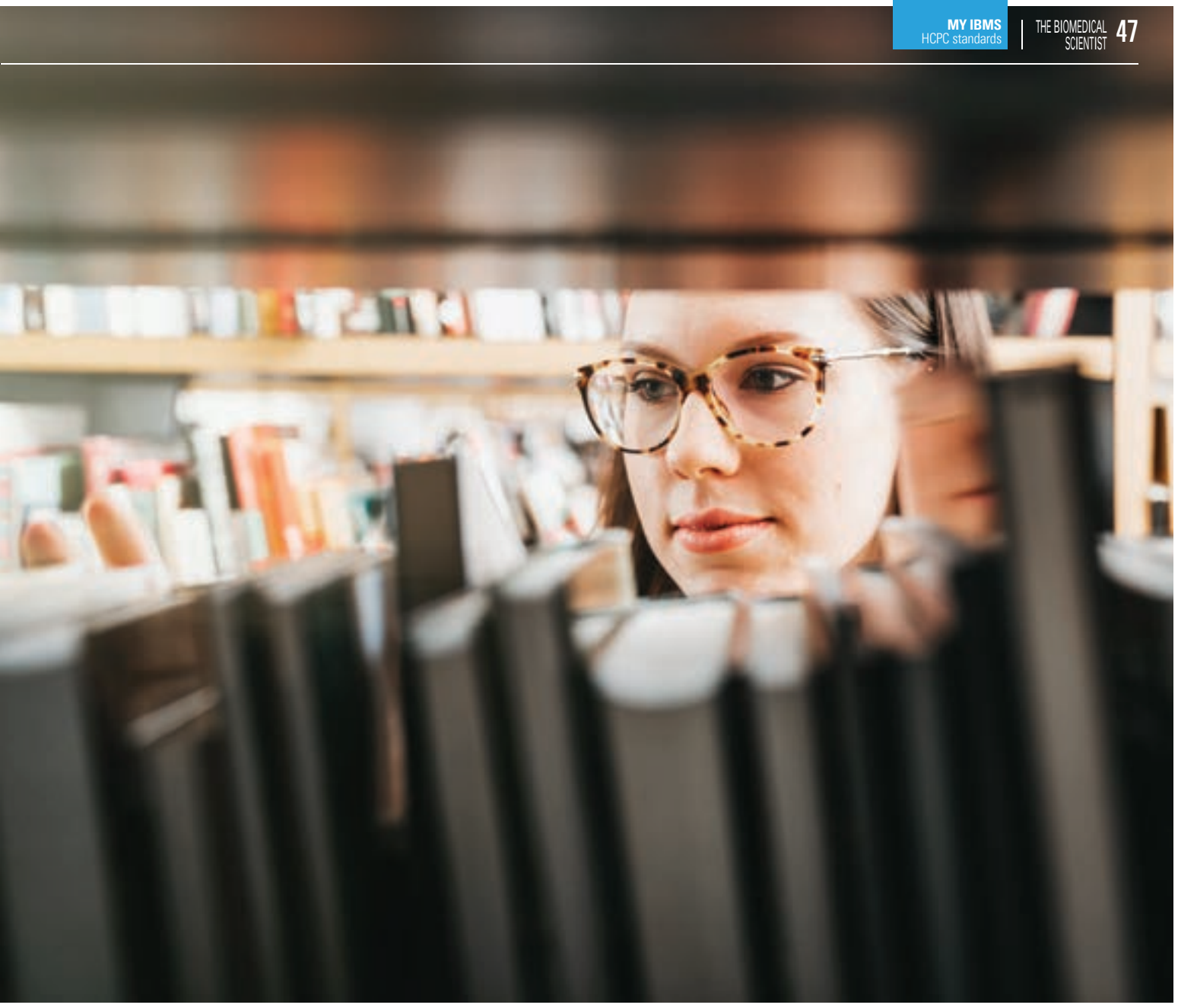
Each year the HCPC conducts an audit to ensure ongoing compliance with the SETs, which were last revised in 2017. This year the HCPC also asked for extra evidence to show how we monitored practice-based learning, how service users and carers have been involved in the programme and its effectiveness, as well as feedback from relevant programme stakeholders relating to these areas, and how we have used this to make improvements.

In responding to the audit, a number of revisions were identified for the IBMS processes that will be implemented from September 2019. These are primarily to the registration training portfolio, application forms and verification/monitoring forms. A brief summary is provided below. Please note they will only affect those who enrol on programmes from September 2019. They do not affect those who are allocated portfolios before this date.

SET 3.6 There must be an effective process in place to ensure availability and capacity of practice-based learning for all learners.
Accredited degrees containing the Registration Training Portfolio have processes for agreeing training capacity with employers each year and this is checked through the annual monitoring process. The other IBMS programmes apply to those who are in employment so capacity for practice-based learning is embedded in their IBMS-approved training programmes. In the case of the equivalence routes for biomedical scientists and clinical scientists, evidence they meet the standards of proficiency comes from prior learning, training and experience.

SET 3.8 Learners must be involved in the programme.
Learners are already able to feed into our programmes in a number of ways, for example: student involvement during accreditation visits, as student representatives on university programmes, feedback on the external verification process. We also follow up any electronic feedback we receive and include any suggestions in the discussions and reviews that regularly take place within the IBMS education team and inform revisions to our processes and guidance information.

SET 3.16 There must be thorough and effective processes in place for ensuring the ongoing suitability of learners' conduct, character and health.
SET 4.2 The learning outcomes must ensure that learners understand and are able to meet the expectations of professional behaviour, including the standards of conduct, performance and ethics.
SET 6.2 Assessment throughout the programme must ensure that learners demonstrate they are able to meet the expectations of professional behaviour, including the standards of conduct, performance and ethics.
Knowledge and understanding of the expectations of professional behaviour (informed by the IBMS code of conduct) and the HCPC standards of conduct, performance and ethics have always been fundamental to training of biomedical scientists, and these standards are already being met in a number of ways. There is now greater emphasis on not just knowing but demonstrating application in practice. Greater signposting of the requirement of evidence will be introduced, together with



"These changes are essential to the IBMS maintaining its HCPC approval status"

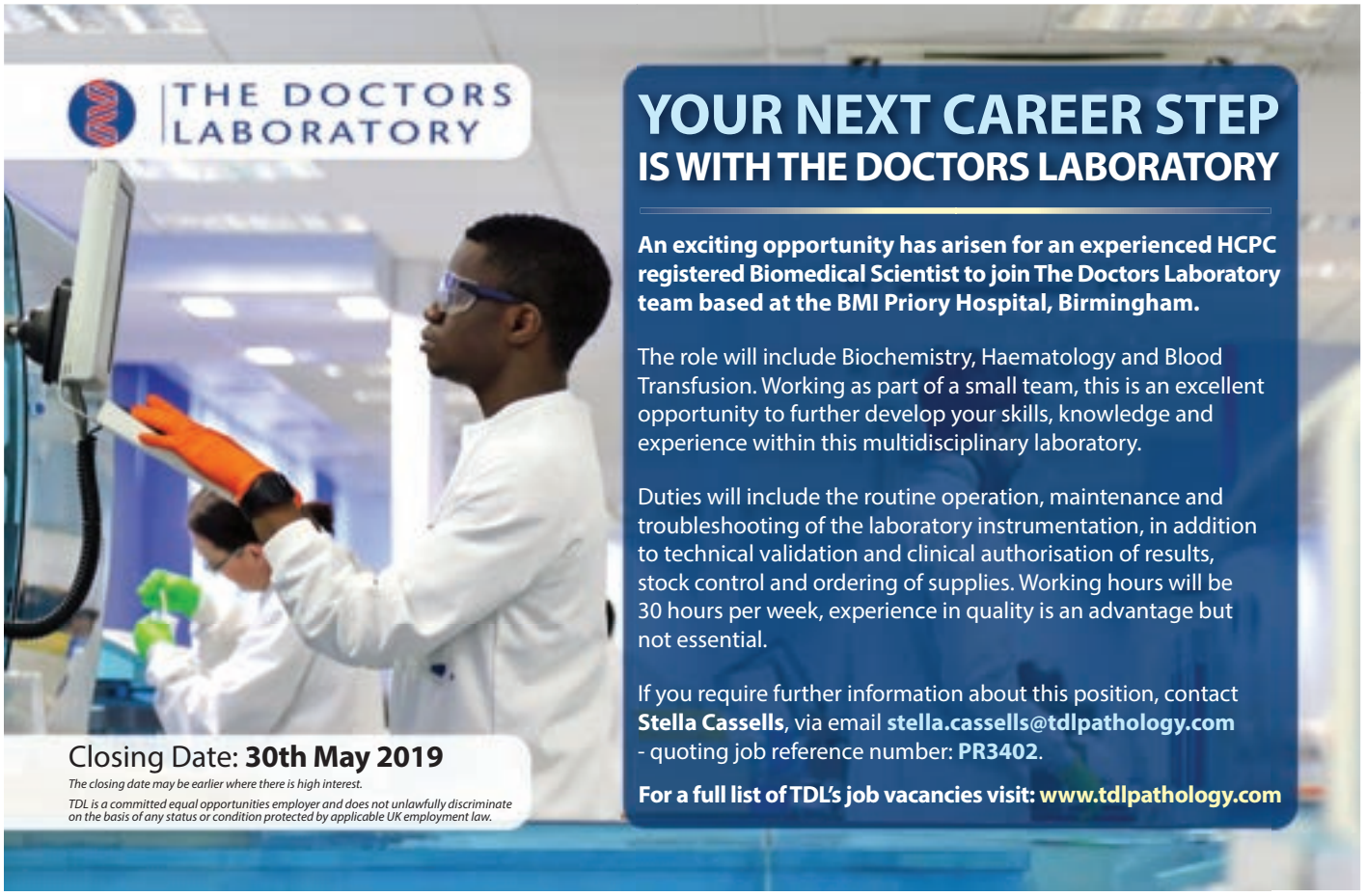
monitoring of compliance through the portfolio verification application form and the External Verifiers Report.

SET 3.17 There must be an effective process in place to support and enable learners to raise concerns about the safety and wellbeing of service users. Crucial to this SET is demonstration of supporting learners if they wish to make a complaint. To strengthen how this SET is met, external verifiers will question trainee biomedical scientists about this on external verification visits. Trainees will also be required to complete a Points of Contact section within the Registration Portfolio for all programmes.

SET 4.9 The programme must ensure that learners are able to learn with, and from, professionals and learners in other relevant professions. Interprofessional interaction and learning is fundamental to our programmes due to the interprofessional working of biomedical scientists within the pathology team and wider healthcare community. However, this SET is now about learners having the opportunity to learn from professionals and learners from other relevant professions.

To strengthen the assessment a mandatory reflective statement requiring candidates to comment on what they have learned from other professionals will be introduced in 2019 for completion of the Registration Portfolio in all programmes.

These changes are essential to the IBMS maintaining its HCPC approval status as an education provider and demonstrates a commitment to ensure those who qualify to become registered healthcare professional through the IBMS are able to practise their profession safely and effectively.



UK Clinical Laboratory Product Specialist (LS)

Ortho Clinical Diagnostics

Position Summary

Ortho UK have two new positions for UK Clinical Laboratory Product Specialist; one in the North and South of the UK respectively.

The UK Clinical Laboratory Product Specialist is a key member of the local Ortho team working with the Sales, Marketing and Administration teams. The LS delivers the implementation of projects, instrument set-up and supports equipment and product use for Ortho Clinical Diagnostics customer base.

The LS schedules workload, support visits within UK to minimize system down time and maintain high level of customer satisfaction. The LS role is the key technical contact point on all aspects concerning the application of troubleshooting of instrument software or hardware issues, ensuring implementation projects are delivered as per standard SOPs as well as the training requirements for the customers.

Major Duties & Responsibilities

- Responsible for ensuring technical aspects of implementations are planned, initiated and completed in an efficient and timely manner using available internal and external resources in line with standard operating procedures.
- Key technical contact point for Clinical Laboratory within a specified territory including all aspects concerning the application of troubleshooting of instruments, software or hardware issues, and training requirements for the customers.
- New instrument performance qualification where required by contract and by customer.
- Support all systems to the designated product performance metrics and KPIs associated to service contracts within Ortho Care.
- Supports sales teams with customer interaction of new account opportunities, including technical presentation of Ortho technical capabilities (instruments, software. Develops menu opportunities with existing customers.
- Responsible for following Ortho complaint handling procedures relative to complaint identification, documentation, resolution, and escalation.
- Provides operational guidance for the day-to-day effectiveness of the Ortho Care team including co-ordination of installation activity, coordinating / assisting with National troubleshooting scenarios, working with team to ensure modifications are installed by due dates. Acts as the subject matter expert on PSS CL activities.
- Participates in any required new software / hardware evaluations. Sets up and maintains processes /documentation used by the Ortho Care team.
- Works closely with TSM to uphold open clear communications across the Ortho Care Team maintaining and leveraging the team's skills and knowledge to meet the business needs and plan.

The Individual:

- Educated to a recognised academic and technical standard dependent on Country requirements and policies
- 2 years working in a hospital/industrial laboratory environment as a Biomedical scientist (or equivalent) in the core laboratory setting (Clinical chemistry / immuno-assay)
- Familiarity with dry slide technology would be an advantage.
- Good verbal, non-verbal and written communication skills
- Knowledge of the organization and management of the healthcare and laboratories structure
- Knowledge of the market and the competition and the ability to compare and contrast their products with Ortho products is an advantage
- Must also have a demonstrable knowledge and understanding of the fundamentals of project management.
- Ability to operate in a team environment as well as working on own is important
- A full clean driving license is essential

To apply please visit www.orthoclinicaldiagnostics.com/en-us/home/Careers

MY LAB

DYNAMIC HISTOPATHOLOGY SERVICE

Trainee Specialist Biomedical Scientist **Megan Clarkson** gives a guided tour of her laboratory at Salford Royal NHS Foundation Trust.

Salford Royal NHS Foundation Trust is part of the Northern Care Alliance, known for its deliverance in safe, high-quality and reliable care to all the local communities and residents it serves. The trust's mantra, "saving lives, improving lives", is something we do with excellence. A recent merger with Oldham Hospital resulted in a larger geographical reach, which allows the pathology services to share and expand on best practice, rolling it out to all service users and patients in providing the best quality care and enforcing our mantra on a wider scale.

The histopathology department is the Greater Manchester centre for neuropathology, upper GI surgery, and sub-regional centre for dermatology and renal medicine. These specialist disciplines require the brightest in the field to run and maintain the service. I am proud to say the staff in the department are just that. They comprise a diverse, dynamic and dedicated workforce, which handles the pressures of a busy specialist lab with grace. The department consists of 15 pathologists, 21 biomedical scientists, 11 receptionist and 14 laboratory assistant staff, who go above and beyond the call of duty to help maintain the ISO 15189-accredited service, while running an additional core routine histology and electron microscopy service.

My role involves rotation through all aspects of the routine histology service, including handling renal and muscle biopsies, frozen sections, a broad range of immunocytochemical tests and special stains on a monthly rota basis. The department makes use of 4 BenchMark Ultra platforms used for an array of over 150 diagnostic prognostic and predictive antibodies. We also provide an in-house DDISH service, with excellent breast core turnaround times. The laboratory is currently in the validation process of a new PDL1 antibody to add to our repertoire. The laboratory is expecting new equipment in the coming months, some of which includes four new tissue processors and the Ventana special stains machine.

The department is an IBMS-accredited training laboratory, offering training and development opportunities in the form of registration, specialist, higher specialist and dissection portfolios, amongst others. I am currently undertaking my Specialist Portfolio and Masters at the same time, which is something that I would not be able to do without the positive support network the department has.

We collaborate with Lancaster University in order to give students the opportunity to gain invaluable experience, both theoretically and practically, in a real-life working environment as part of their undergraduate degree. The department receives consistent positive reviews and feedback from service users, patients and staff, reiterating the hardworking, positive and uplifting environment that we thrive in at Salford Royal.

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