ONE-TO-ONE

MAN VERSUS MACHINE

Can algorithms be as effective as human radiologists? *p.16*

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IS MORPHOLOGY DEAD?

The future of blood films goes under the microscope: *p.26*

WORKFORCE EQUALITY

INCLUSIVITY?

LGBTQ issues in the NHS and pathology over 40 years: *p.34*

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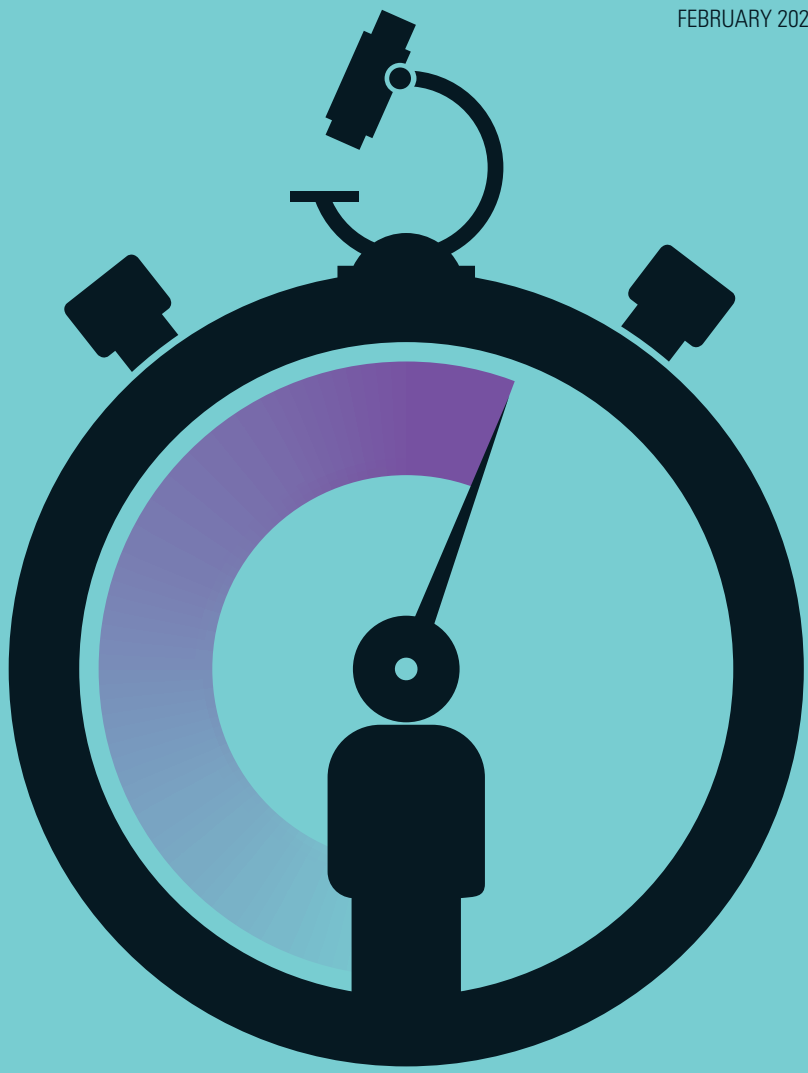
FEBRUARY 2020



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INNOVATIONS IN CELLULAR PATHOLOGY

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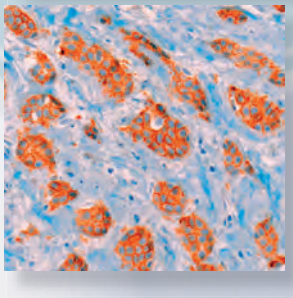

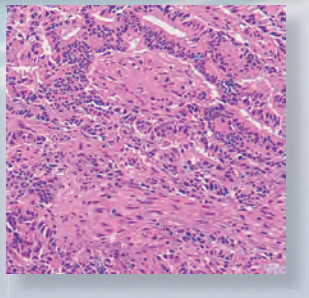

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DEALING WITH CONFLICT

Sarah May, IBMS Deputy Chief Executive, on the damaging effects of conflict and the hope of change

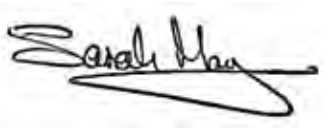
Human history is peppered with wars, conflicts and individual vendettas and despite all the hopes and aspirations that accompanied the dawn of the new millennium, here we are, two decades in and the world is in an unwanted political maelstrom of probably the greatest magnitude since the Second World War.

I have been watching in horror the aftermath of the assassination of Iranian General Qasem Soleimani. By the time this article appears in print I am hoping that common sense will have prevailed and that all sides will have pulled back from an attack and counter-attack strategy and that communication and diplomacy are seen as the preferred and more constructive way forward from a dangerous situation. At this moment, we are still poised in a waiting game to see if either side is about to launch a salvo upon the other; irrespective of allegiances, I do not think "pistols at dawn" is the best way to resolve a deeply difficult and highly charged situation.

There is surely not a single person reading this who has not witnessed the damaging and long-lasting effects of conflicts, whether in the laboratory, between friends or within families. There is not a magic formula for solving relationship problems, whether between nation states or individuals, particularly if the opposing sides hold radically and diametrically opposing views, and fisticuffs, even of a high-tech military nature, rarely solves anything. It still comes down to good old low-tech dialogue and diplomacy.

Throughout my working life the thing I have found most damaging, and difficult to manage, has been interpersonal conflicts. They have a nasty, pernicious habit of poisoning a whole environment and creating a highly unpleasant working atmosphere, not just for those immediately concerned, but also for those in the wider environment. I think my greatest professional achievements have not been of a scientific nature, but have been the occasions I have been able to pull someone away from a destructive behavioural path and helped them to understand the impact of their actions and for me to perhaps help others to understand the reason for their behaviour.

This leads me on to an article in this month's edition that I found profoundly moving; it is the piece by Colin Mudd about his experience over 40-plus years in pathology as a gay man, and of the changing attitudes towards LBGTQ individuals. It left me feeling good about our workforce, a workforce that has grown in its attitudes and one that is tolerant and accepting. Perhaps if there were more individuals in the world like Colin and his many colleagues, tolerance and acceptance would be the norm and we wouldn't be in the mess that we find ourselves in at this moment.



Sarah May
Deputy Chief Executive

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DIAGNOSTIC DIVISION

HISTORY DRIVEN BY INNOVATION

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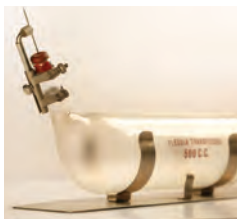
1909



1929

1987

1996

2016

2017

GRIFOLS HAS MORE THAN A 100-YEAR HISTORY OF COMMITMENT TO SCIENTIFIC DISCOVERY, IMMUNOHEMATOLOGY DIAGNOSTICS, AND TRANSFUSION MEDICINE.

HIGHLIGHTS OF GRIFOLS MILESTONES IN BLOOD SAFETY:

1909 The first clinical analysis laboratory "Instituto Central de Análisis Clínicos" is established.

1929 Dr. Grifols designs a safer, indirect method to conduct blood transfusions in Spain through the invention of the "transfusion flebula". It enables blood to be stored temporarily using anticoagulant solution.

1940 Laboratorios Grifols is established.

1945 Grifols pioneers the opening of the very first private blood bank in Spain and helps to set up Spanish regulations with the goal to screen donors to ensure the safety of the blood supply.

1960 Grifols commercializes diagnostic reagents in Spain, in partnership with Dade Reagents, and starts developing the Coombs centrifuge and other immunohematology instruments.

1984* Chiron is first to clone and sequence the HIV genome, enabling progress on diagnosis and treatment of AIDS.

1987 Diagnostic Grifols is established.

1988* Chiron scientists discover and publish Hepatitis C virus, enabling a new generation of life-saving tests and treatments.

1996 Grifols launches the first generation of gel cards.

1999* Chiron launches the first Procleix system and 2-in-1 NAT HIV/HCV assay to detect HIV and Hepatitis C in donated blood and plasma.

2002* Chiron develops Procleix West Nile Virus assay to address a new threat to the blood supply.

2004* Grifols launches the second generation of gel cards, the DG Gel cards.

Procleix Ultrio assay is the first 3-in-1 NAT blood screening test for detection of HIV and Hepatitis B and C.

2010 Grifols launches Erytra, the next-generation immunohematology auto analyzer for high-throughput DG Gel processing.

Progenika Biopharma grants Grifols worldwide exclusive distribution of its BLOODchip products for Blood Group Genotyping.

2014 Grifols acquires Novartis Diagnostics.

2016** Grifols develops the Procleix Zika Virus assay to address a new threat to the blood supply.

Grifols establishes a new Immunohematology Center in San Marcos, TX, where we provide specialized testing and education.

2017 Grifols acquires Hologic's NAT donor screening.
Erytra Eflexis gets the CE mark.

2019 Procleix Panther system featuring ART (Automation Ready Technology) gets the CE mark.

* In addition to its own pioneering work, Grifols is proud to share and steward the legacy of Chiron, a company that made key advances in immunohematology.
** The Procleix Panther system, and the Procleix Zika assay are for Investigational use only in the US. The performance characteristics of these products have not been established.

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SCIENCE NEWS IN NUMBERS

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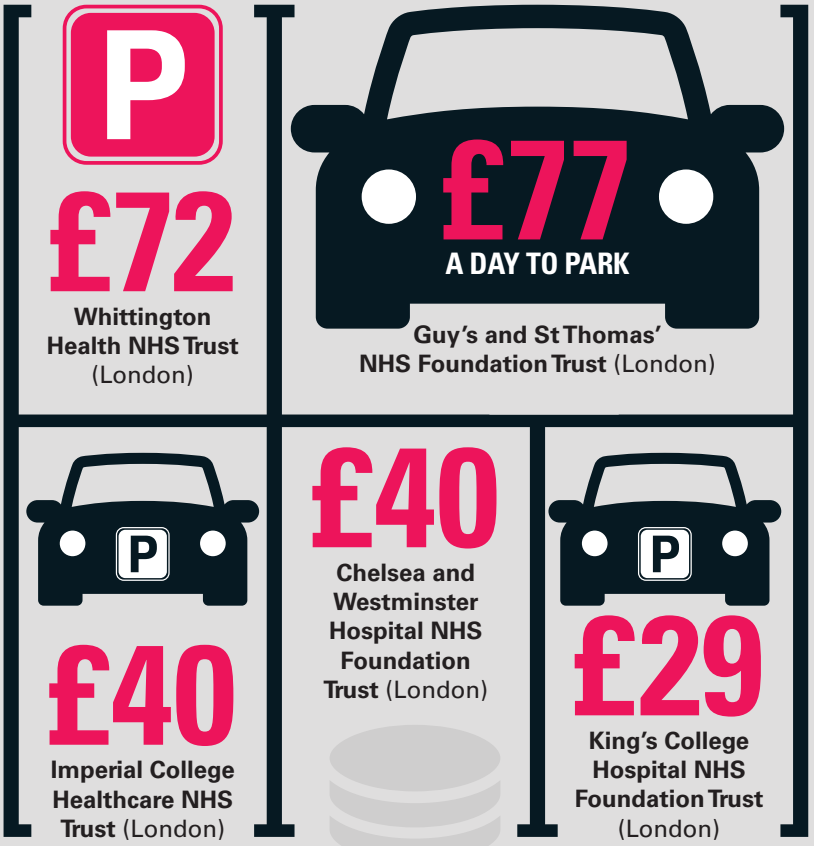


BLOOD DONATIONS

For every 100 women who started giving blood in 2019, just 70 men did the same.

Only **41% of new donors** were **men** last year. **NHS Blood and Transplant's target** for **new male donors** has now **increased by 26%** for this year.

Hernia mesh implants

100

New data shows more than 100 different types of mesh were purchased by NHS Trusts from 2012 to 2018 in England and Scotland, leading to fears over safety.

The meshes can **cut into tissue and nerves**, leaving some people **unable to walk, work or care for children**. Regulator the **MHRA** said there is a clinical need for the devices.

9 YRS

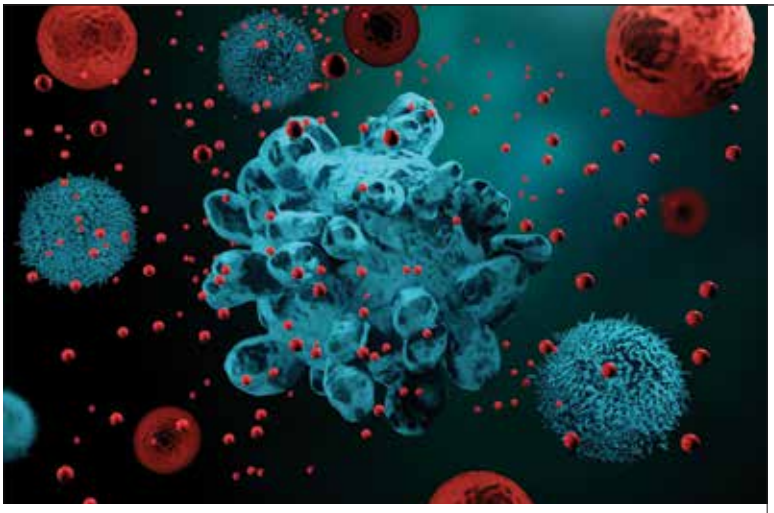
Being wealthy adds nine years to healthy life expectancy, according to transatlantic research.

It includes **data from 10,754 UK adults aged 50 and older**, and **14,803 US adults over 50**. The paper shows that at **50, the wealthiest men in England and the US** lived about an **additional 31 healthy years**, compared with about **22 to 23 years** for those in the **poorest wealth groups**.

1 in 6

One in six women who lose a baby in early pregnancy experiences long-term symptoms of post-traumatic stress, a UK study suggests.

Imperial College London and **KU Leuven** in Belgium looked at 650 women, of who **29% showed symptoms of post-traumatic stress one month after pregnancy loss**, declining to 18% after nine months. Most had been through an **early miscarriage before 12 weeks**, while the rest had an **ectopic pregnancy**.



SCIENCE NEWS

BLOOD CLOTS

Exosomes after a stroke

A stroke appears to create a sticky situation inside the blood vessels of the brain that can worsen damage days, or even months, later.

Scientists found that after a stroke, exosomes travelling in the blood get activated and sticky and start accumulating on the lining of blood vessels.

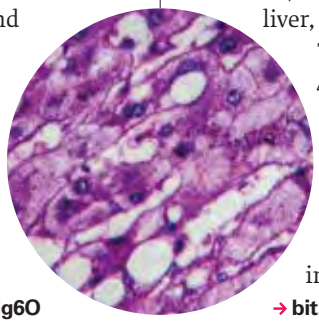
Platelets, which enable blood to clot after an injury, start adhering to the now-sticky exosomes, causing a buildup that can effectively form another clot.

The scientists have also shown (in both stroke models and human blood vessels) that exosomes moving through the blood then pick up the unique and normally sticky peptide sequence, arginine-glycine-aspartate (RGD), which can cause additional brain damage.

More typically, exosomes carry a negligible amount of RGD, a protein that's important in holding together the extracellular matrix that helps cells connect and form tissue.

In the aftermath of a stroke, cells and the extracellular matrix both get damaged, and sticky RGD is set free.

→ **go.nature.com/2RdMg6O**



POPULATION-BASED STUDY

FATTY LIVER DISEASE

One in five young adults has fatty liver disease (steatosis), with one in 40 having already developed liver scarring (fibrosis), research has found.

The study is the first to attempt to determine the prevalence of fatty liver disease and fibrosis in young healthy adults in the UK.

Fatty liver disease is broadly split into non-alcoholic fatty liver disease (NAFLD), which is usually seen in people who are overweight or obese, and alcohol-related fatty liver disease.

If left untreated both can lead to fibrosis (scarring of the liver) and, in severe cases, eventually cirrhosis of the liver, which is irreversible.

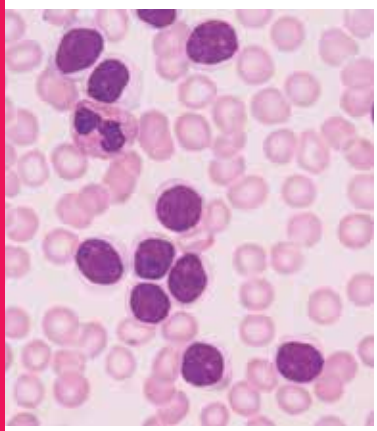
The research looked at data collected from 4021 participants of the Children of the 90s study, also known as the Avon Longitudinal Study of Parents and Children.

Researchers first looked at those participants who did not report harmful alcohol consumption and found that one in five had NAFLD.

→ **bit.ly/2G6lp4T**

STEM CELL TRANSPLANT

RESEARCH INTO RARE GENETIC MUTATIONS IN DONORS' STEM CELLS



A stem cell transplant is a common treatment for blood cancers, such as acute myeloid leukemia (AML).

Such treatment can cure blood cancers, but also can lead to life-threatening complications, including heart problems and graft-versus-host disease, in which new immune cells from the donor attack a patient's healthy tissues.

A study shows that extremely rare, harmful genetic mutations present in healthy donors' stem cells, though not causing health problems in the donors, may be passed on to cancer patients receiving stem cell transplants.

The intense chemotherapy and radiation therapy prior to transplant and the immunosuppression given after allow cells with these rare mutations the opportunity to quickly replicate, potentially creating health problems for the patients who receive them, suggests the research.

The study, involving samples from patients with AML and their stem cell donors, suggests such rare, harmful mutations are present in surprisingly young donors and can cause problems for recipients even if the mutations are so rare as to be undetectable in the donor by typical genome sequencing.

The research opens the door to a larger study that will investigate these rare mutations in many more healthy donors, potentially leading to ways to prevent or mitigate the health effects of such genetic errors in stem cell transplant patients.

→ **bit.ly/2NHZIDa**

IMAGES: ISTOCK/SHUTTERSTOCK

RAPID DIAGNOSIS CENTRES

SLASHING WAITING TIMES FOR CANCER DIAGNOSIS

A rapid diagnosis centre has cut waiting times for patients with non-specific symptoms who may have cancer from 84 days to six.

It also costs less than current standard care, if used at more than 80% of capacity, new research has shown.

The study is the first complete cost-effectiveness analysis of rapid diagnosis centres (RDCs).

RDCs are now being established within the NHS, building on experience in Denmark. They are aimed at the large number of patients who have vague and non-specific symptoms that could be due to cancer, but who do not meet the criteria for urgent referral.

The researchers evaluated the RDC in Swansea Bay University Health Board (SBUHB), which has been running since June 2017 at Neath Port Talbot Hospital. Patients are referred to the RDC by their GPs.

The researchers found that average time for a cancer or non-cancer diagnosis, or to discharge from the clinic, was reduced from 84 days in usual care to under six days, if the diagnosis is made at the RDC appointment.

If further investigations are arranged in the RDC, the time to diagnosis is just over 40 days.

As long as the RDC runs at 80% capacity or over, it is less costly, as well as more effective, than standard clinical practice.

→ **bit.ly/2G6p443**

6 DAYS

A **RAPID DIAGNOSIS CENTRE** HAS **CUT WAITING TIMES** FOR PATIENTS WITH **NON-SPECIFIC SYMPTOMS WHO MAY HAVE CANCER** FROM **84 DAYS TO SIX**.

WHAT'S HOT AND WHAT'S NOT

HOT

SILICA

Engineered ingestible molecular traps created from mesoporous silica particles introduced to the gut can have an effect on food efficiency and metabolic risk factors.

HOT

GUT BACTERIA

Bacillus subtilis, which boosts digestive health, could slow and potentially even reverse the build-up of protein associated with Parkinson's, new research suggests.

HOT

SEX

Women who engage in sexual activity weekly or monthly have a lower risk of entering the menopause early, according to a new University College London study.

NOT

BLOOD PLATELETS

Research reveals how a clotting protein and blood platelets can promote cancer progression and suppress immune responses to cancer.

NOT

GLASSES

Six in 10 Swedish people over 70 could improve their vision by getting eyeglasses or changing the power of the glasses they already have, according to a new study.

NOT

SUGAR

Sugar influences brain reward circuitry in ways similar to those observed when addictive drugs are consumed, according to Danish research.

MICROBIOLOGY

CELLS KEEP TOGETHER FOR PROTECTION

Cell-to-cell contacts are necessary for the survival of human cells under protein-damaging conditions and stress.

This was a conclusion reached by a research team from Åbo Akademi University, who said they were surprised by the findings, because the molecules they studied are usually linked with other cellular functions.

Lea Sistonen, Professor in Cell and Molecular Biology, said: "Our results show, for the first time, that the contacts between cells, known as cell adhesion, are essential for cells to survive stress.

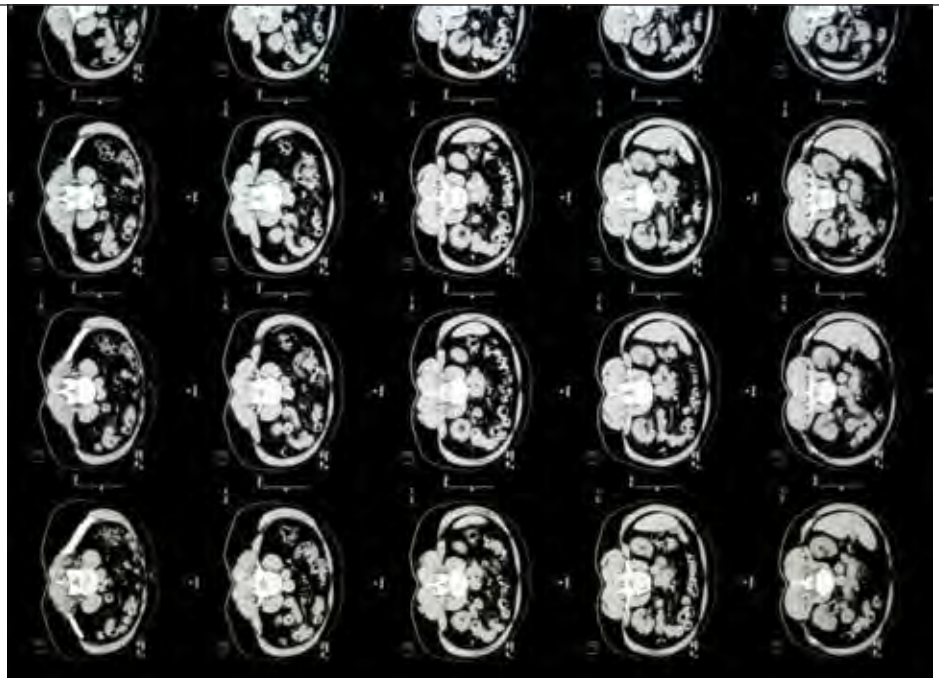
"The findings also suggest that impaired cell adhesion may sensitise cancer cells to drugs that damage cell proteins and cause stress."

The research project focused on heat shock factor 2 (HSF2), a specialised gene-regulating protein, and its impact on cells' capacity to survive protein-damaging stress.

Protein-damaging stress is caused by, for example, high temperatures, virus infections and certain anti-cancer medications.

The results showed that HSF2 contributes to protecting cells against stress by regulating those genes that mediate cell adhesion contacts.

→ **bit.ly/2G6plhZ**



CANCER METABOLISM

PULLING THE PLUG ON PANCREATIC CANCER

UK scientists have identified a new way to kill pancreatic cancer cells by "pulling the plug" on the energy generator that fuels calcium pumps on their cell surface. They report how switching off the cancer's energy supply causes the pancreatic cancer cells to become "poisoned" by an irreversible build-up of calcium.

Calcium inside cells is normally beneficial as it controls numerous cell functions. However, calcium levels are tightly controlled and normally kept at very low levels, as prolonged elevations in calcium lead to cell death.

This tight control is achieved by calcium pumps on the cell surface that use chemical energy to pump calcium out of the cell.

The scientists discovered that switching off the cancer cells' energy supply causes these pumps to fail and calcium to rise, effectively poisoning the cell.

→ **go.nature.com/38srkyK**

NEUROBIOLOGY

ARE BIGGER BRAINS BETTER?

When it comes to certain parts of the brain, bigger doesn't necessarily mean better.

A larger hippocampus (a curved, seahorse-shaped structure embedded deep in the brain) does not always reliably predict learning and memory abilities in older adults.

It's normal for the hippocampus to shrink as we age and scientists previously believed that a bigger hippocampus meant a better memory.

A 2004 study showed that its size does not always matter for memory in older adults and a new study sheds light on why.

It indicates that the size or volume of the hippocampus is only a meaningful marker of learning for older people with more intact limbic white matter – the neural circuitry that connects the hippocampus to the rest of the brain.

Andrew Bender, lead author of the paper, said: "Our findings highlight the need to measure not just the size of the hippocampus, but also how well it's connected to the rest of the brain when we look for

physical markers of memory decline in older adults."

The study has potential implications for earlier diagnosis of ageing-related memory disorders, such as Alzheimer's disease.

Some older adults whose brain scans show a larger hippocampus could have their cognitive decline overlooked or mischaracterised if physicians do not also consider their white matter connectivity.

→ **bit.ly/2G9XrH3**

GLOBAL RESEARCH

"Sepsis causes one in five deaths"

Twice as many people as previously believed are dying of sepsis worldwide, according to a new analysis.

Among them are a disproportionately high number of children who are from poor areas.

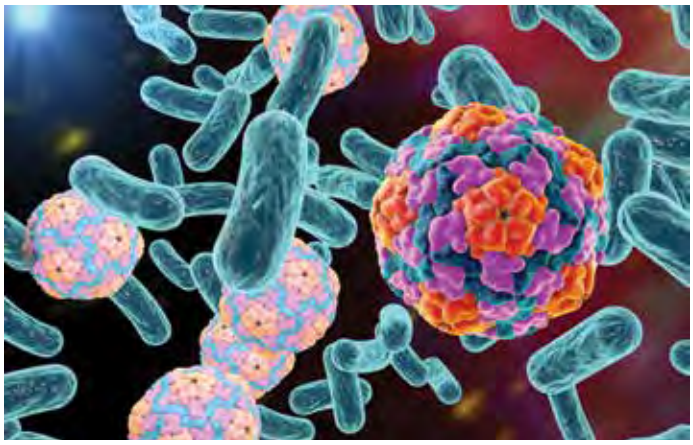
Led by researchers at the medical schools of the University of Pittsburgh and the University of Washington, the study revealed 48.9 million global cases of sepsis in 2017 and 11 million deaths, representing one in five deaths worldwide.

The majority of sepsis – 85% – occurred in countries with low- or middle-sociodemographic status.

The highest burdens were found in sub-Saharan Africa; the South Pacific islands; and South, East, and Southeast Asia.

Sepsis incidence was higher among females than males and peaked in early childhood, with more than 40% of cases in children under five.

Dr Mohsen Naghavi, senior study author, said: "We are alarmed to find sepsis deaths are much higher than previously estimated, especially as the condition is both preventable and treatable.



"We need renewed focus on sepsis prevention among newborns and antimicrobial resistance – an important driver of the condition."

For their analysis, Naghavi and colleagues leveraged the Global Burden of Disease study, a comprehensive epidemiological analysis, which reports on 282 primary causes of death, not including sepsis, which is considered an intermediate cause of death. A primary cause of death is the underlying condition (such as cancer), which leads to the intermediate cause (sepsis) that ultimately results in death.

Previous estimates were limited because they relied upon hospital databases from a select group of middle- and high-income countries.

The new findings are unprecedented as they represent mortality both in and out of the hospital.

→ **bit.ly/2TI8yiK**

EDUCATION

INTERNET USE AND MOTIVATION

New research shows that students who use digital technology excessively are less motivated to engage with their studies. This effect is made worse by the increased feelings of loneliness that use of digital technology produces.

A total of 285 university students enrolled on a range of health-related degree courses participated in the study, which was conducted at Swansea University and the University of Milan.

The study found a negative relationship between internet addiction and motivation to study.

Students reporting higher levels of addiction also found it harder to organise their learning productively.

→ **bit.ly/2tzRXmn**

UNDER THE MICROSCOPE

This month: Elongation of Very Long Chain Fatty Acids Protein 2

What on earth is that?
It's the admittedly lengthy name of a protein-coding gene, which we will shorten to ELOVL2 for ease.

I'm assuming this has been in the news?
Yep. Scientists carrying out research on mice have identified the role that it plays in the ageing of the eye.

What did they find out?
An age-related decrease in ELOVL2 gene expression was associated with increased DNA methylation of its promoter.

What is methylation?
The process by which groups of carbon and hydrogen atoms are transferred from one substance to another. In the case of DNA, methylation of regulatory regions negatively impacts expression of the gene.

So what happened in the study?
When researchers reversed hypermethylation *in vivo*, they boosted ELOVL2 expression and rescued age-related decline in visual function in mice.

What does that mean?
It indicates that ELOVL2 actively regulates ageing in mouse retina and provides a molecular link between polyunsaturated fatty acids elongation and visual functions. It suggests novel therapeutic strategies for treatment of age-related eye diseases.

Is this protein coding gene found in humans as well?
Yes, it is. And it regulates levels of docosahexaenoic acid (DHA), a polyunsaturated omega-3 fatty acid abundantly found in the brain and retina. DHA is associated with a number of beneficial effects.

What happened next?
The lead author behind this work said: "I have been asked whether I think ELOVL2 is the ageing gene. After thinking about it, it is not unreasonable to think that lower ELOVL2 expression might be the basis for many age-related conditions. Future work in our lab will address that question."

IMAGES: ISTOCK/SHUTTERSTOCK

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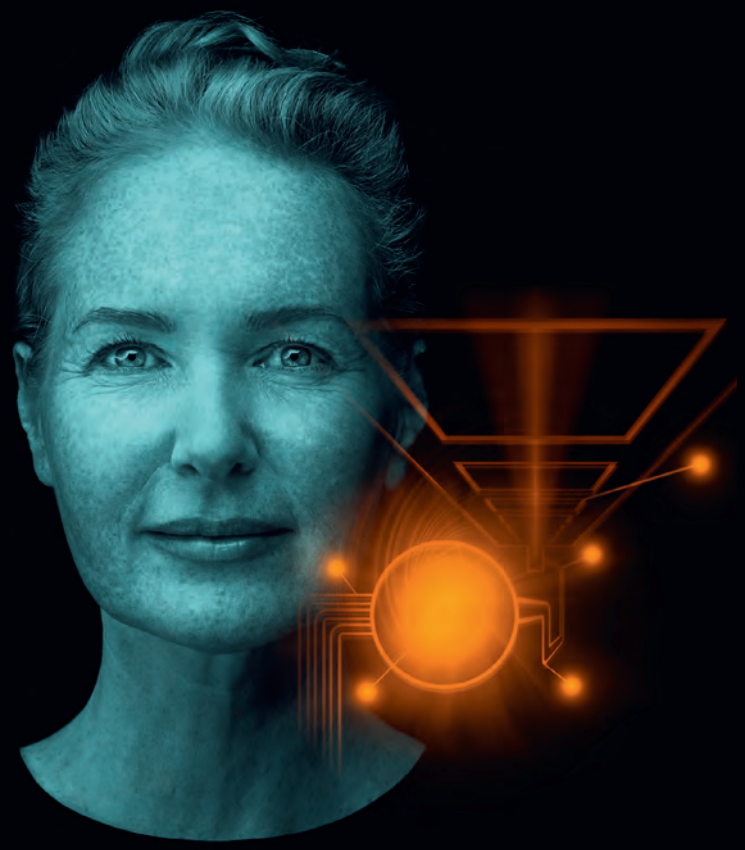

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siemens-healthineers.co.uk/rapidpoint500e

SIEMENS Healthineers

TECH NEWS

SYNGENE

PCR WORKSTATIONS

Syngene, a manufacturer of image analysis solutions, is now supplying the AirClean AC600 series of PCR workstations.

Some of the workstations include HEPA filtration and all use UV irradiation to minimise risk of airborne DNA contamination, saving time by producing consistent quality DNA from their PCR.

Syngene's AC600 series PCR workstations feature sturdy polycarbonate cabinets with built-in 254 nm UV lighting to irradiate surfaces.

→ **syngene.com**

PROMEGA

GENOME EDITING

Promega has signed a license agreement with MilliporeSigma to access MilliporeSigma's foundational CRISPR genome-editing technology.

Under the agreement, Promega will create new research products for investigating endogenous biology, including those for drug development. These will allow researchers to better read the physiological or natural levels of protein expression, providing a more accurate understanding of protein behaviour.

→ **promega.co.uk**

MAST GROUP

CARBAPENEMASE DETECTION

The new Mast Isoplex cre-art kit for the rapid molecular detection of carbapenemase-producing organisms has been launched.

It delivers rapid results with 15 minutes hands-on time and 30 minutes run time. It's ready-to-use, with lyophilised pellets containing all primers and reagents and highly sensitive and specific, giving confidence in results.

It is a loop-mediated isothermal amplification kit for the detection and characterisation of the seven most prevalent carbapenemase families.

→ **mast-group.com**

THE BIG QUESTION

THIS MONTH WE ASK

"How could antibiotics be used more responsibly?"

Jonathan Lewis

Laboratory Manager
Department of Microbiology
Gloucestershire Hospitals NHS Foundation Trust

Unfortunately, there is no easy answer to this question. Each country can do its bit, but antibiotic resistance is a truly global problem.

It is not uncommon for resistance to develop in areas of the world where there are overcrowded populations and overuse of antibiotics. These conditions are perfect for bacteria to be exposed to the pressures needed for resistance to develop. Resistant bacteria are then carried to other countries as people travel.

As individuals, we can play our part in preventing resistance from getting worse, and protecting some of our current antibiotics. Two of the most important factors are only using antibiotics where necessary and making sure to complete a prescribed course, if given. The number of new antibiotics being developed by the drug companies is low, due to the costs involved and the risk of a limited return on investment. This means we have to protect the ones we are using now. Antibiotics are also used widely for veterinary and agricultural purposes and there is evidence of cross-over resistance developing. Countries with tighter controls on antibiotic use in animals tend to have a lower rate of resistance in human bacteria.

It's too easy to take antibiotics for granted. We have all been fortunate to live in a time when antibiotics are freely available and still effective against infections. However, the balance is starting to shift in the wrong direction.

IMAGE: ALAMY

Phillipa Burns

Trainee Consultant Clinical Scientist HSST
Hull University Teaching Hospitals

Antibiotics are arguably one of the greatest health inventions of the last century – a successful adjunct to vaccines in the prevention of infectious disease.

Their potency has dwindled due to the evolution of antimicrobial-resistant organisms, inextricably linked to increased antimicrobial prescribing. The decision to prescribe is often made before microbiology results are available; our current diagnostics are too slow to impact prescribing practice.

Some centres, like ours, have adopted molecular syndromic testing panels to improve accuracy of diagnosis, but they are costly. We need rapid, simple diagnostics to enable the right drug to be prescribed for the shortest time possible.

Antimicrobial stewardship is crucial for the health of the individual patient and for the wider health of the population; it preserves what we have now for the future. We enforce this message through ward rounds, encouraging a switch from broad-spectrum to narrow and shortening courses, we know this tactic can spare the gut microbiota and remove a selection pressures that drive resistance. Unfortunately, our work is focused on hospital patients and we have no real influence on community prescribing – we need to do more.

As scientists we can make a difference by supporting the adoption of rapid diagnostics, pledging to be antibiotic guardians and engaging with the British Society of Antimicrobial Chemotherapy, which offers free membership!

Michael Palmer

Laboratory Manager
National Mycology Reference Laboratory
Public Health England/North Bristol NHS Trust

It is widely understood that the over-prescribing and inappropriate use of antibiotics has led to the emergence of resistant organisms and, in some instances, multi-resistant strains.

There is plenty of evidence to suggest that antimicrobial resistance increases with the length of exposure an organism has to a particular agent. Despite this, the general advice is to finish a course of treatment, an area which deserves more research. Evidence from the World Health Organization suggests that for some infections shorter antibiotic courses may be effective while reducing an organism's exposure and thereby the development of resistance. In the meantime, however, a more targeted approach to antimicrobial prescribing is required, enlisting the help of the microbiology laboratory to provide specific antibiotic profiles that can support robust antimicrobial stewardship programmes to inform decision-making.

Reducing the number of infections is possible by using vigorous cross-infection protocols and vaccination in both human and animal settings – hence reducing the need for antimicrobial treatment. Other stakeholders can play their part and the patient should take their medication as prescribed and not share unfinished antibiotics with family or friends.

Doctors and vets should only prescribe antimicrobials if they are necessary and, where possible, based on laboratory results, while agricultural use should be restricted, and governments must be involved in international plans.

MAN VERSUS MACHINE

Hutan Ashrafian outlines a project that proved a computer algorithm to be as effective as human radiologists in spotting breast cancer from x-ray images.

As a preventative measure, the mammogram has been a big success. It has caught countless cases of breast cancer early, giving treatment the best possible chance. It's not perfect though and now a multi-disciplinary team of clinicians, neuroscientists and software engineers has developed an algorithm that could read mammogram x-rays at least as accurately as expert human radiologists.

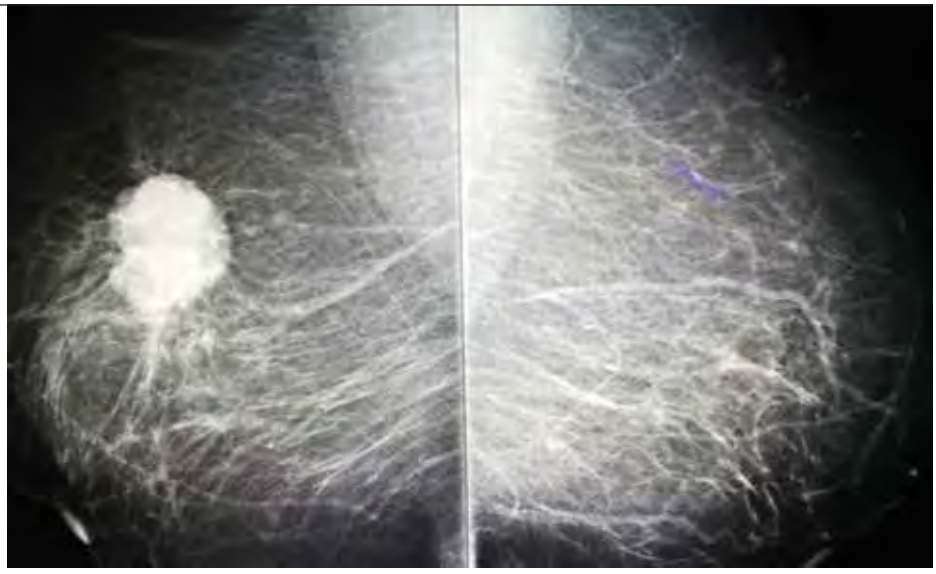
Reading a mammogram requires a high degree of knowledge, skill and experience. It can be a challenge and that means it is also subject to error, resulting in false positives and negatives. Given the sheer number of images that radiologists have to interpret – here in the UK alone, the NHS screened 2.2 million women in 2016-17 – the potential for misinterpretation is considerable. In some cases, mistakes create unnecessary anxiety for women. In other cases, it means the opportunity to catch the disease early has been missed.

Translating data

Overcoming this weakness was the aim for the research team drawn from Google Health, DeepMind, US hospitals, NHS hospitals and Imperial College London. Their raw material for the project was a large dataset of almost 26,000 images from a Cancer Research project in UK hospitals and a smaller set of 3000 images from a handful of US hospitals.

One of the key authors of the report was Hutan Ashrafian, Chief Scientific Advisor and Clinical Lecturer in surgery at Imperial College London, who has been involved in the project from its inception.

"The aim of this work from day one was to take a dataset that could be translated into a digital format and then used in a way that would give the maximum benefit to women called in for routine mammogram screening," he says. "The mammogram is the best modality we have today for reducing the massive burden of breast cancer. Screening is the strongest way to manage the disease via early diagnosis and treatment. The point of this research, then, was to augment the screening programme, and to support the people working in that programme. There are not enough radiologists, and



with an ageing population the numbers are only likely to get larger, so our objective was to look at the potential for a digital solution."

Analytical platform

With developments in the world of machine learning moving at a pace, the hunt was on for an industry partner that could spearhead the development of a suitable analytical platform. It came in the shape of DeepMind, the innovative UK company of AI experts, which during the project became an integral part of Google Health. Along with the clinical experts and an expansive stock of images, the pieces for the project were now assembled. "All these stakeholders came together," says Hutan. "The job then was to see if we could come up with a way to support the health system to manage these millions of mammograms."

The success of the project would depend on the quality of the AI that DeepMind could devise, which in turn depended on the quality of information that underpinned it. The two image datasets were one key strand of this, the other was the clinical expertise. "We gave the AI experts the protocol of selection, the parameters for false positives and negatives, the baseline of what is cancer and what isn't, and so on," says Hutan. "It was an intricate process that involved the whole group, including people who take the mammograms."

What was the margin of error that the AI would seek to improve? "Depending on which dataset you look at, of 100 women screened, four might have a queried image. But only one of those might actually have cancer. So there needs to be an increase in accuracy for the whole process."

Promising results

Better accuracy is precisely what the AI system delivered. For false positives it gave an absolute reduction of 5.7% on the US dataset and 1.2% on the UK dataset. For false negatives the reduction was 9.4% and 2.7%, respectively. The AI was also tested as part of the double-reading process used in the UK (where one radiologist reads the image and gives a verdict, and a second confirms the result). Here, the AI was found to be non-inferior and could potentially cut the workload of the second reader by up to 88%.

The results look promising. "It might even be better than that," says Hutan, "because the algorithm had access to the images and nothing else, whereas the radiologists had access to patient details and history. So they were working from more knowledge than the AI."

The big question now is not whether AI will play a major role in medicine, but how long before it is widely used in clinical settings. Hutan says: "Something like 25% of radiology research now involves an AI element of one sort or another. I think it is an inevitable innovation. Its real potential is to augment processes in terms of sensitivity and to reduce mortality and unnecessary interventions. In this case, we are looking at a more accurate and quicker turn around of the scans, and that would also free up the capacity of the radiologists who read these mammograms to concentrate their skills on more pressing matters."

To Hutan's mind, the timeframe for this is not the next 25 years, but far sooner. "The pressing question is how do we get this approved through the national regulatory bodies? We have the AI, now we want to take it to clinical trials and then show efficacy at a national level. We have already started the discussions with Public Health England, NHS Improvement and so on. Ideally, we would like to see it operating in one form or another in the next two to three years." BMS

2.2m HERE IN THE **UK ALONE**, THE **NHS BREAST SCREENING PROGRAMME** SCREENED **2.2 MILLION WOMEN** IN 2016-17 – THE **POTENTIAL** FOR **MISINTERPRETATION IS CONSIDERABLE**.

HUTAN ASHRAFIAN

- ✔ **1990s:** Bachelor of Science, Bachelor of Surgery, Imperial College London
- ✔ **2001:** House Officer, surgery and urology, Royal Free London
- ✔ **2002:** Doctor in A&E, Barts
- ✔ **2007:** Honorary Registrar, Imperial College London
- ✔ **2006:** Registrar Surgeon, Great Ormond St Hospital
- ✔ **2015:** PhD, Imperial College London
- ✔ **2015:** Senior Registrar in bariatric and metabolic surgery, Chelsea and Westminster Hospital
- ✔ **2017:** Honorary Senior Clinical Fellow in surgery, Chief Scientific Advisor, Institute of Global Health Innovation, Imperial College London

IMAGES: SHUTTERSTOCK

REDUCING TURNAROUND TIME

DELIVERING REAL-TIME PCR IN HISTOPATHOLOGY

Clinical Scientist and Molecular Pathology Lead **Siobhan Taylor** looks at the experiences of implementing a new platform within a routine histopathology service and the impact it has had on patient care.

In October 2018, the histopathology laboratory at Gloucestershire Hospitals NHS Foundation Trust (GHNHSFT) introduced a new platform for rapid molecular testing of formalin-fixed paraffin-embedded (FFPE) tissue. Following a period of in-house verification, we have introduced testing in melanoma (BRAF mutation) and colorectal cancer (KRAS, NRAS, BRAF mutations and microsatellite instability (MSI) testing). Implementation of this benchtop platform has enabled us to reduce turnaround times for delivering molecular pathology results, with a beneficial impact on patient care.

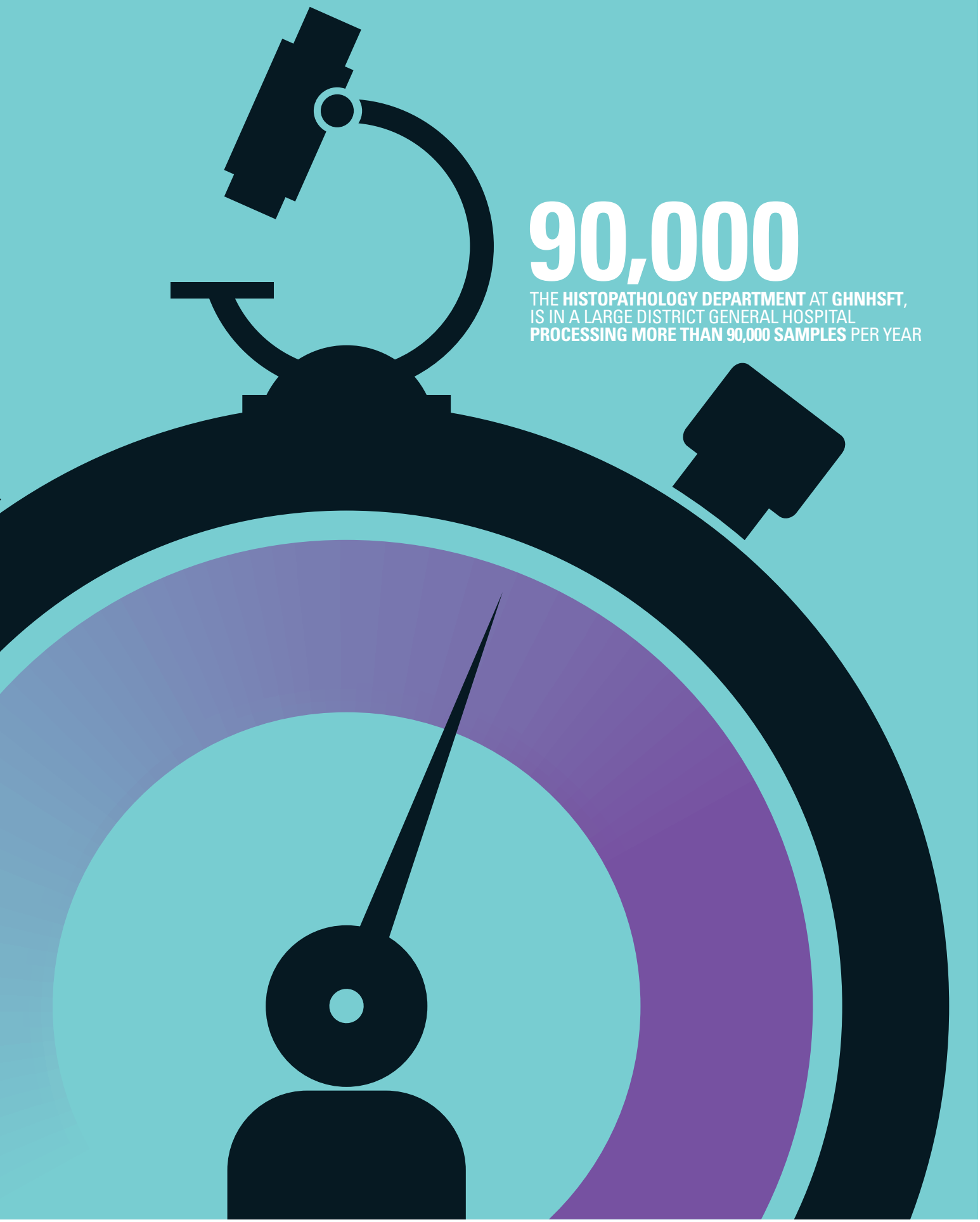
Histopathology and molecular pathology

The histopathology department at GHNHSFT is in a large district general hospital serving a population of ~900,000, processing more than 90,000 samples per year. Complex molecular testing of patient tumour samples, to aid in diagnosis and subclassification, prediction of response to therapies and identification of therapeutic targets, is traditionally performed in specialist genetic laboratories.

Molecular testing of samples received by our laboratory is largely outsourced, which can lead to delays in patient treatment. Turnaround times are extended due to the time taken to ship the samples and reliance on an external laboratory's workflow for testing and reporting.

Verification

There are a number of different assays (CE-IVD and RUO) available to use on the platform for the detection of a number of mutations in both FFPE and liquid biopsies in different tumour types. In our laboratory, we have explored the use of FFPE to date.



90,000

THE **HISTOPATHOLOGY DEPARTMENT** AT **GHNHSFT**, IS IN A LARGE DISTRICT GENERAL HOSPITAL **PROCESSING MORE THAN 90,000 SAMPLES** PER YEAR

TABLE 1. VERIFICATION OF CARTRIDGES PERFORMED AT GHNHSFT

Test	Time	Min.% neoplastic cells	# verified	External controls	Concordance	Service Go-Live
BRAF	90 mins	50%	17	2x V600E standard 1x V600K standard	100%	March 2019
KRAS	120 mins	10%	13	2x multiplex 1x A59T (50%)	100% *	May 2019
NRAS/BRAF	120 mins	10%	10	None Retro Prospective	100%	September 2019
MSI		20%	23	Yes	91.3% **	TBC

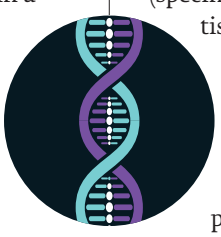
*: one specimen with a mutation not present in the KRAS mutation test was run during the verification and showed a negative result.
**: Two of the 23 cases verified for the MSI assay showed a disconcordant result. This was investigated by the system provider and concluded to be a true but rare occurrence.

The assay cartridges are extensively validated by the manufacturer, and discussion with other users suggested variability in what individual laboratories had undertaken for their own verification. For our quality control (QC) purposes, we verified the individual assays separately, using both externally sourced controls and a selection of at least 10 historic clinical cases with a known result.

These included specimens from a range of sample sizes (small biopsies vs large resections and whole section vs macro dissection) and percentage neoplastic cell content (including samples that were at the limit but not below the manufacturer recommendations) to test the platform capabilities and prove accuracy.

We began with verification of the BRAF mutation test in melanoma samples, using a retrospective approach, and were able to "go live" with a service fairly rapidly. We verified the KRAS mutation test in colorectal cancer samples in a similar manner, but the NRAS/BRAF mutation assay proved more challenging, due to a lack of previously tested colorectal samples for BRAF mutation. Therefore, we used a combined retrospective and prospective approach, testing samples in-house and sending them away for external verification to assure the result, which slightly delayed implementation of a full service for colorectal cancer.

We have also verified the MSI assay, comparing previously obtained mismatch repair (MMR) immunohistochemistry (IHC) results for the colorectal cancer specimens tested. Table 1 summarises the verification performed for each cartridge.



Neoplastic cell content

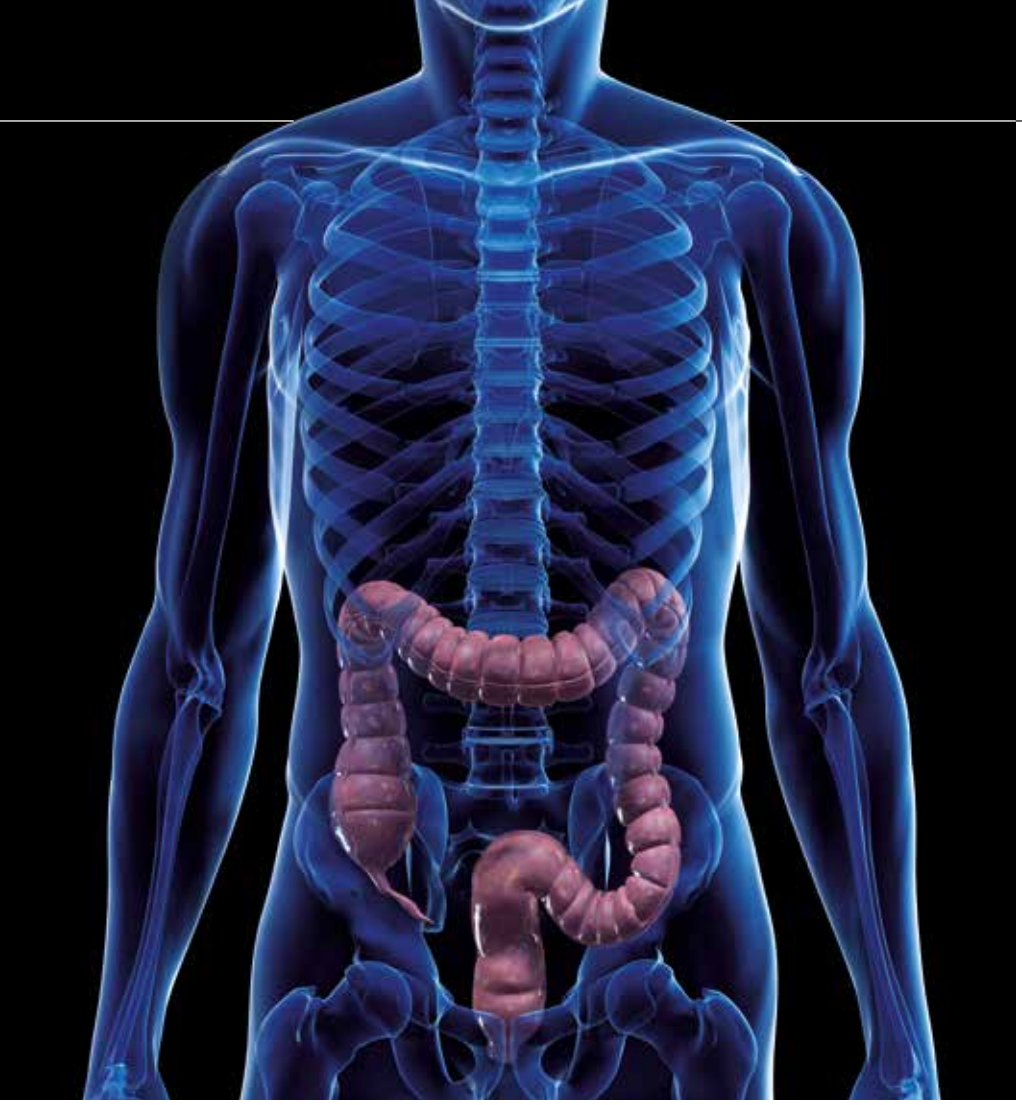
All specimens for molecular testing must first have their neoplastic cell content assessed. This should be performed on a section taken immediately prior to that which will be tested. At the time of selecting suitable cases for verification, a fresh H&E was taken on all potential cases to allow estimation of the percentage neoplastic cells present in the sample, assessment of tissue suitability (specimen size, necrosis, remaining tissue) and marking of the area containing neoplastic cells. To ensure a systemic approach, the pathologists involved undertook the tumour assessment e-learning programme by the Genomics Education Programme.

During the verifications, a number of samples were disregarded as they were assessed to contain insufficient material. We remain unable to test samples that do not meet the minimum requirements for the indicated assays, most often due to insufficient available material. In these instances, we continue to outsource these samples for alternative testing in our specialised referral laboratory. However, in the future we have the option to validate the use of smaller samples on the platform.

Sample preparation

The platform is a closed system and as such, clean and accurate working is imperative to ensure the integrity of the result. Misidentification and/or contamination of the sample at any point has the potential to lead to the incorrect assignment of a result, which could ultimately lead to a patient receiving the incorrect treatment. During the pre-analytical phase, we therefore consider it imperative that stringent measures are in place to reduce the possibility of sample mix-ups or cross-contamination.

These precautions apply to the preparation of all material for molecular techniques, whether performed



IMAGES: ISTOCK/SHUTTERSTOCK

"Depending on the assay performed, a result is available between 90 and 150 minutes"

in-house or externally. Introduction of this new technique in our laboratory has raised awareness as to how specimens referred for molecular technique should be handled.

We have found it useful to have a dedicated microtome in a "clean" area, away from disruption and potential contaminants. We utilise clean microtomy techniques when preparing samples for all molecular pathology requests, which requires cleaning of all equipment, tools and surrounding work bench with 70% IMS prior to use and in between sample blocks. Clean gloves and a clean laboratory coat must also be worn, and a fresh section of blade must be utilised for each new sample.

When taking sections, we adopt a one-block-only policy at the microtome to ensure the correct patient material is sampled. DNAase-free tubes are labelled with specimen details to allow clean transport from the microtome to the Idylla workspace. In our laboratory, we have generated new request sheets to encompass this work, which allow us to document and record each step and ensure the relevant QC checks are performed and countersigned by a second member of staff.

During the verification period, we used a cleanly prepared water bath for the preparation of all samples, with no apparent issues. However, on one occasion since, we have experienced a problematic result, which could not be resolved by external testing.

A thorough examination of our processes highlighted the water bath and brush as a potential source of contamination and we have since ceased this practice when preparing material for the platform. We are now able to macrodissect sections either at the microtome, or on a clean glass slide.

Loading and running

The footprint of the platform is such that it requires only a small clean space to work, which has been key to enabling us to fit it into our limited laboratory workspace. The loading of the sample into the assay cartridge is the same for all FFPE assays, involving the formation of filter-paper "sandwich" to contain and load the sample, using small aliquots of nuclease-free water. This step takes a couple of minutes, while use of our newly-generated worksheet allows for second checks at each stage to ensure traceability.

Results

Depending on the assay performed, a result is available between 90 and 150 minutes. The system automatically interprets the results, generating a console result report, which can either be downloaded onto a memory stick, or downloaded from the platform's software.

In our experience, the generated reports are easy to interpret; in addition to containing all relevant QC information, the report for each sample tested includes a clear genotype result, which mutation has been detected, the protein HGVS and the base change. This information is clearly displayed in the report to enable replication to our own pathology report.

The software allows visualisation and some limited interrogation of the PCR curves generated from the test. Following on from our verification period, and as we have gained more experience and confidence with the platform and software, we now also perform a detailed check of the PCR curves. In checking the wild-type total Cq value of the assay as an indication of the overall quality of the sample and, for mutation positive samples, the ΔCq value, we aim to ensure added confidence in the results obtained. This has involved extensive support from the platform supplier team, who have been incredibly patient and informative.

In line with any molecular technique, the manufacturer states that fixation of

samples should be limited to 24 hours, after which degradation of DNA can occur, affecting result outcome. In practice, this is hard to restrict in a busy histopathology laboratory, and our laboratory information system does not allow for accurate monitoring of fixation. However, we have not yet experienced any problems with DNA degradation/integrity of our own clinical samples. Indeed, other studies have shown the platform performs better on samples of poor quality where other techniques might fail.

Reporting

Reports generated for molecular pathology testing are complex and require the inclusion of specific detailed information, but follow a standardised approach with a similar principle to histopathology reports that utilise the Royal College of Pathologists datasets.

My discussion with other users of the platform indicated no consensus for who should/could report results generated from this testing. Some laboratories assume a traditional histology workflow, with consultant pathologists reporting. Others adopt an health care scientist (HCS) reporting workflow strategy. As a department, we currently adopt a dual HCS/pathologist reporting strategy, while we familiarise ourselves with the technique; an HCS compilesmand oversees the report and a pathologist checks and authorises it. In the near future, following appropriate training, we will be extending the neoplastic cell content assessment and reporting/authorisation processes to a scientist role only, which will reduce the impact on the consultant pathologist and increase scientist scope of practice.

External quality assessment (EQA)

Participation in a national EQA scheme is recommended for ISO 15189 accreditation purposes. We have chosen to register with the relevant Genomic Quality Assessment schemes for the assays we are currently running, which assess both the result produced and the report generated. We have also established an internal QC timetable.

Fixation of samples should be limited to 24 hours, after which degradation of DNA can occur, affecting results

Turnaround times

The introduction of in-house molecular testing for clinically relevant mutations in melanoma and colorectal cancer has positively impacted turnaround times for many patients in our region, ensuring results are available within a few days, compared to one to two weeks. We have received direct feedback from our clinical teams that patient anxiety is reduced with the availability of all relevant results prior to starting treatment. We also have evidence of situations where particularly poorly patients have benefited from earlier access to treatment with the availability of a rapid result. Such urgent testing of samples, when necessary, is not possible when samples are outsourced.

In-house testing also ensures that patient material remains in the laboratory and is easier to locate should further testing be required and, where limited material is available, it is possible to make an informed decision on how it is best used.

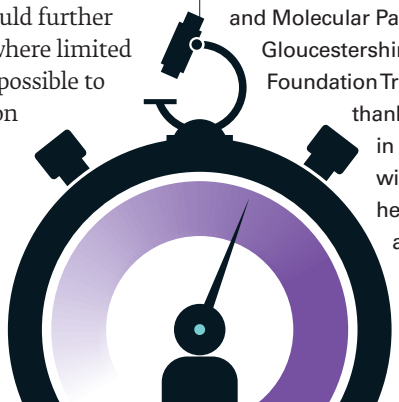
Conclusions

The implementation of the platform within our trust has allowed us to further strengthen the delivery of personalised medicine in a timely and effective manner to the patients in our region, directly impacting patient care.

It has proven easy to use and generates rapid results. We have achieved excellent concordance with known results during verification and continue to be very pleased with the results generated by our service. The introduction of this testing within our laboratory is increasing staff training and knowledge and expanding the roles of scientists within a histopathology laboratory. The scientist team within the laboratory has been able to collaborate with wider teams across our trust, improving inter-departmental relationships and delivering cost savings.

We have implemented a new technique within our laboratory, which has proved challenging at times, however, the application of strict pre-analytical procedures has ensured confidence in our results. While we have not experienced any issues with the DNA quality of our samples, we are learning to recognise quality results and, where infrequently we have experienced cartridge problems, we have experienced excellent customer support from the product supplier teams.

The current restructuring of genomic services into seven genomic laboratory hubs may see a time restriction on our use of this platform. Whatever the future for this testing, it is without doubt that the knowledge and expertise held within histology laboratories will remain crucial to molecular pathology techniques. BMS



Siobhan Taylor is a Clinical Scientist and Molecular Pathology Lead at Gloucestershire Hospitals NHS Foundation Trust. She would like to thank colleagues at GHNHSFT in the laboratory and the wider clinical teams for their help and support. To see the article with references, visit **thebiomedicalscientist.net**

THAWING BLOOD

Quality and Training Supervisor Tola Elegbe on thawing times and haemostatic assessment.

There is growing demand for plasma to be more rapidly available for the management of major bleeding, although the recent approval of extended shelf life of thawed fresh frozen plasma (FFP) to 120 hours has addressed this and improved the early availability of plasma for adult patients during major haemorrhage and has reduced unnecessary wastage. But studies show that the haemostatic qualities of FFP deteriorate when the shelf life of a thawed component is extended beyond 24 hours.

Therefore, it could be argued that the impairment in haemostatic qualities of extended thawed FFP could translate to lesser efficacy in the management of major bleeding, although clinical studies are required to confirm this.

In the case of paediatric patients who are bleeding, FFP components (methylene blue-treated FFP (MBFFP) and solvent detergent FFP (SDFFP)) are still thawed on demand, because their shelf life remains 24 hours after thawing.

This means that in these patients the national recommendation for delivering a 1:1 ratio of FFP with red cells in trauma bleeding situations is not met.

New technologies

Recently, there has been an increased interest in replacing fibrinogen early (with cryoprecipitate) for the treatment of major haemorrhage associated with trauma and obstetrics. The current shelf life of cryoprecipitate after thawing is four hours, and *in vitro* data from NHS Blood and Transplant has confirmed that its shelf life could be extended for up to 72 hours from the haemostatic qualities point of view. However, unlike extended thawed FFP, extended thawed cryoprecipitate will need to be kept at room temperature and, therefore, there is a potential risk for bacterial growth.

The ideal situation would be to have a faster thawing method than the current method, which would allow for quicker delivery of plasma to patients and thawing of plasma on demand to reduce unnecessary wastage, as even with the availability of extended thawed FFP we will not be able to eliminate wastage. It would also mean better quality (and safer) plasma components for patients.

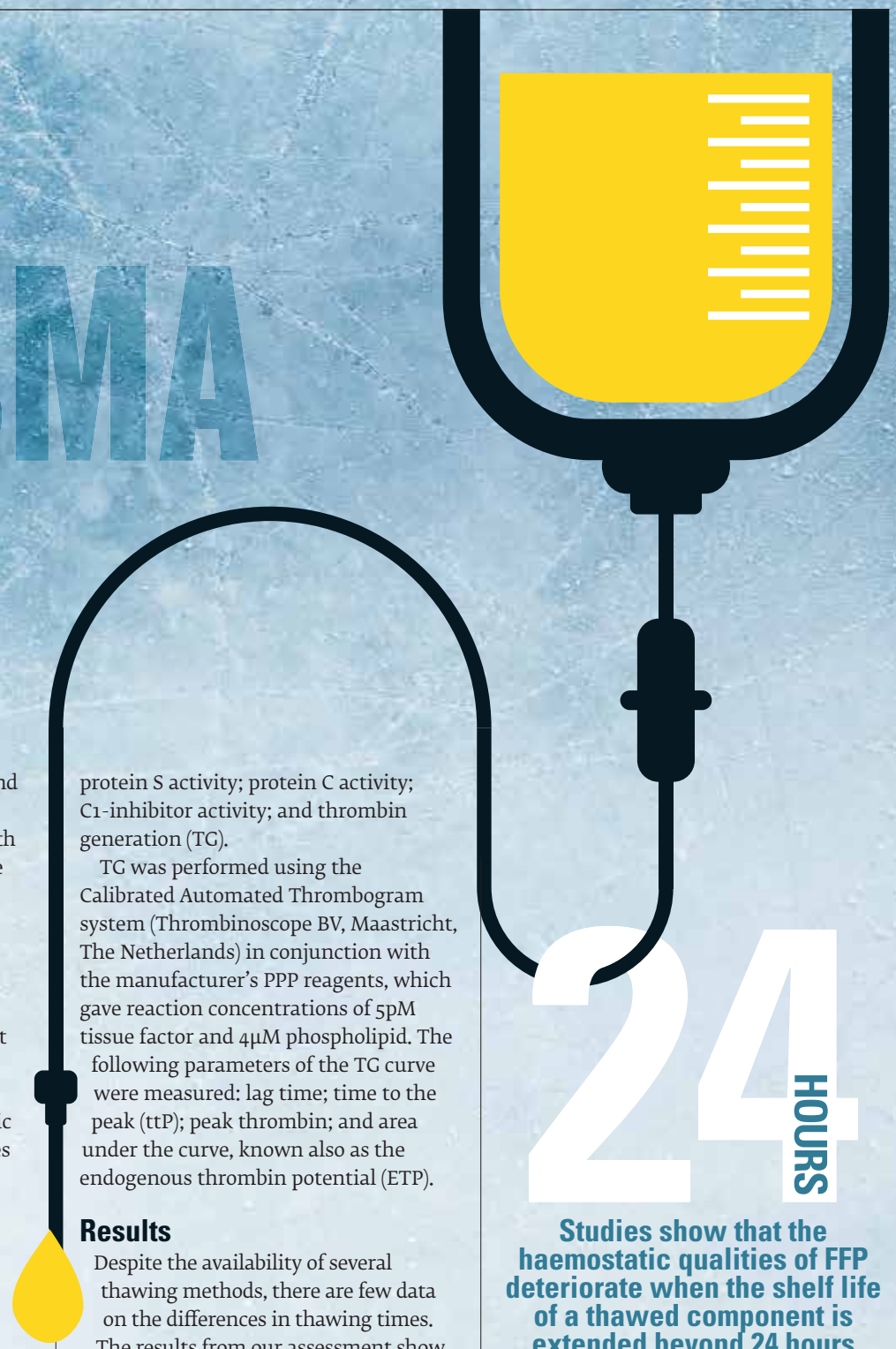
"New technologies on the market are capable of thawing plasma at up to 45°C"

The recommended temperature for thawing plasma products is 37°C, but new technologies on the market are capable of thawing plasma at up to 45°C. This could contribute to faster thawing times making plasma more rapidly available for the management of major haemorrhage. Barkey has developed the plasmatherm, a water-based plasma thawer with the ability to thaw frozen plasma in 15 minutes, using a temperature range of 37°C to 45°C, and for smaller volume components, such as cryoprecipitate and paediatric units, the thawing time can be further reduced, if temperatures higher than 37°C are used.

Assessment of thawing times

For a thawing-time assessment, four FFP units were thawed in the Barkey plasmatherm at 37°C. Assessment of thawing times was performed by two biomedical scientists to prevent bias. After five minutes, the units were examined visually and physically to check for ice particles and if the units were appropriately thawed and suitable for issue to patients. If they were not adequately

PLASMA



thawed, they were left in the thawer and checked again at seven, nine, 11, 13 and 15 minutes. This was then repeated with new units of similar volumes using the Barkey plasmatherm at 45°C and the ThermoGenesis ThermoLine at 37°C.

Assessment of haemostatic capacity

LG-octaplas is a pooled plasma product and is likely to show less variability of haemostatic effect than FFP, so was used for the assessment of haemostatic capacity. A thawing time of 30 minutes for LG-Octaplas is recommended by Octapharma, so all units were thawed for 30 minutes, for all three arms.

After thawing, LG-Octaplas was stored at 2-4°C and aliquots were taken for haemostatic testing at four different time-points: five minutes after removal from the thawing device (defined as time zero); 24 hours-post thaw; 48 hours post-thaw; and 120 hours post-thaw – the latter timing is the permitted shelf life for thawed plasma in the UK. Samples were stored below -70°C until testing was performed. Assays performed were prothrombin time (PT); activated partial thromboplastin time (APTT); fibrinogen; factor II, V, VII, VIII and XI activity; free protein S antigen; protein S activity; protein C activity; C1-inhibitor activity; and thrombin generation (TG).

TG was performed using the Calibrated Automated Thrombogram system (Thrombinoscope BV, Maastricht, The Netherlands) in conjunction with the manufacturer's PPP reagents, which gave reaction concentrations of 5pM tissue factor and 4µM phospholipid. The following parameters of the TG curve were measured: lag time; time to the peak (ttP); peak thrombin; and area under the curve, known also as the endogenous thrombin potential (ETP).

Results

Despite the availability of several thawing methods, there are few data on the differences in thawing times.

The results from our assessment show that Barkey plasmatherm thawed two units the fastest when used at 45°C and even 37°C, when compared with the ThermoGenesis ThermoLine. However, the ThermoGenesis ThermoLine has the fastest thawing time for FFP when more than two units are thawed. There was no significant difference found when comparing the ThermoGenesis ThermoLine at 37°C and the Barkey plasmatherm 37°C or 45°C in any of the haemostatic properties, when stored for the recommenced shelf life of 24 hours, with the exception of protein S when using the ThermoGenesis ThermoLine. BMS

24 HOURS

Studies show that the haemostatic qualities of FFP deteriorate when the shelf life of a thawed component is extended beyond 24 hours

Tola Elegbe is a Quality and Training Supervisor working in blood transfusion, point-of-care testing and phlebotomy at Barking, Havering and Redbridge University Hospitals NHS Trust.

IMAGES: ISTOCK

"Blood films are still an integral diagnostic tool, which should be used alongside the patient's clinical history and blood count results"

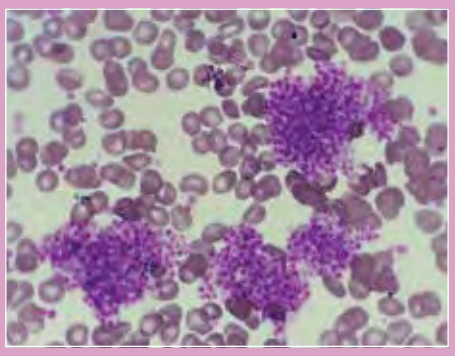
IS MORPHOLOGY DEAD?

Anas Nasir, a Specialist Biomedical Scientist in haematology and blood transfusion, puts the future of blood films under the microscope.

Advancements in technology and other techniques are often conflated with morphology being made redundant. Analysing and reporting blood films is difficult, labour intensive and requires extensive training and experience. Morphological examination may highlight issues with automated analysers and also show things that are currently not detectable by the machines. This article will discuss, with a few examples, why it may be a little early to pronounce the death of blood films.

Platelet clumping

Platelets are integral components of haemostasis, clot formation and they help to stop bleeding. It is, therefore, imperative that accurate platelet counts are provided, as patients have different targets that would determine their need for a transfusion. In a small percentage of patients, platelets clump together due to the commonly used anticoagulant ethylenediaminetetraacetic acid (EDTA) in full blood count samples, resulting in a falsely reduced platelet count or pseudothrombocytopaenia.



This agglutination of platelets is an *in vitro* phenomenon caused by IgG/IgM autoantibodies directed against platelet surface glycoproteins. EDTA exposes epitopes by inducing a conformational change in GPIIb/IIIa and subsequently causes the agglutination to occur. Alternative anticoagulants, such as sodium citrate or heparin, can be used to overcome this issue. Platelet clumping is significant as patients may be subjected to unnecessary platelet transfusions if falsely low counts are reported.

Platelet satellitism

First described by Field and Macleod in 1963 as an *in vitro* phenomenon seen in peripheral blood films, platelet satellitism

is a rare occurrence seen only in blood taken containing EDTA and is absent in other anticoagulants. It is thought that IgG antibodies are formed in the presence of EDTA and directed against the GPII/IIIa complex on the membranes of platelets and the Fc gamma receptor on neutrophils. Coated platelets form a rosette cluster around segmented neutrophils. Platelet satellitism has clinical implications as well as it may result in spurious thrombocytopaenia or pseudothrombocytopaenia, which would require further investigations and interventions. Though satellitism is usually associated with neutrophils, there have also been reported cases of adherence of platelets to lymphocytes and even basophils.

Micro-organisms

The presence of micro-organisms in the peripheral blood can interfere with automated platelet counts, giving a falsely elevated result. Blood film analysis shows certain bacteria to be approximately similar in size and shape to platelets, explaining the error in the automated count. Apart from the bacterial infection, a genuine thrombocytopaenia may indicate other underlying complications such as DIC, for example, which may require further attention.

Red cells simulating platelets

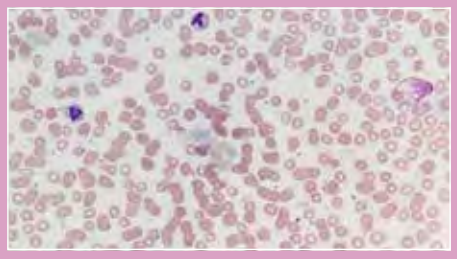
Red-cell fragments (schistocytes) if seen on a blood film require urgent attention, but may also interfere with the platelet count. In patients that have suffered burns, or those with red-cell fragmentation syndromes, fragments may give a falsely elevated platelet count. This can be of clinical significance as in the latter group of patients, an accurate platelet count is essential in the diagnosis and monitoring of thrombotic thrombocytopenic purpura. Burns patients contain microspherocytes and microdiscocytes in their blood that may also be counted as platelets by the analysers.

White-cell fragments

White-cell fragments, though rarely recognised, are quite common and seen in AML and ALL and occasionally lymphoma and hairy cell leukaemia. In a study published in the *Journal of Clinical Pathology*, blood films from 169 patients diagnosed with AML or ALL were reviewed. A 500 particle count was performed and the automated platelet count was compared to what was seen microscopically. More than 5% of "pseudoplatelets" as a proportion of platelets plus pseudoplatelets was regarded as significant and recorded. Pseudoplatelets were seen on the blood films of 25% (43) of the patients. In total, 30% (32/107) of those with AML and 18% (11/62) of patients with ALL had these pseudoplatelets. Retrospective analysis showed that 11 of the 43 patients with pseudoplatelets were thought to be at risk of a major bleeding event. Their automated counts ranged from 10 to 75 x10^9/L but once corrected these dropped to 2-15x10^9/L. Morphologically, these white-cell fragments are comparable to agranular platelets, but with a deeply stained cytoplasm in accordance with the cytoplasm of malignant cells.

Cryoglobulins

Type I cryoglobulins are normally associated with B-cell lymphomas and myeloma, whereas types II and III are associated with infective and inflammatory disorders. Cryoglobulins may falsely increase haemoglobin, platelet count or rarely, white blood cell count, depending on the analyser. Blood film analysis shows precipitates scattered throughout the film, occasionally attached to the red blood cells. The cryoglobulin precipitates sometimes alter the red cell morphology in such a manner that keratocytes may be seen.



Conclusion

Blood films give information that automated analysers are unable to detect or cannot do so properly. These include schistocytes, spherocytes and other poikilocytes, inclusions within red cells or white cells, leukaemic cells or other dysplastic cells. A blood film is usually made in three scenarios: when requested by the clinician, reflex test after a flag or numerical abnormality on the instrument, or just before validation of a full blood count result by the biomedical scientist. Clinically, films may be requested for a vast array of reasons, including unexplained anaemia or jaundice, lymphadenopathy, sickle cell-like symptoms (chest or abdominal pain), pain in bones or joints (may indicate acute leukaemia, sickle cell disease or myeloma) or suspicion of bacterial or parasitic diseases. In the laboratory, the indications for making a blood film are different though just as varied and include an unexplained anaemia or sudden unexplained change in counts, macrocytosis or microcytosis, instrument flags (blast cells, variant lymphocytes), and factitious results for red cell indices. In the laboratory, minimal clinical details are often provided and for unknown patients, it is important to provide a thorough analysis of the features seen on the blood film. The blood film may be the primary diagnostic tool for certain conditions, such as myelodysplastic syndromes, leukaemia and lymphomas. It can facilitate prompt diagnosis and indicate which further tests should be performed. Blood films are still an integral diagnostic tool, which should be used alongside the patient's clinical history and blood count results. BMS

IMAGES: ISTOCK

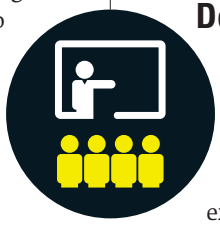
HISTOPATHOLOGY REPORTING QUALIFICATIONS

Dr Joanne Horne and **Dr Bryan Green** look at the Healthcare Scientist Reporting Programme and developing an expert, collaborative histopathology team.

The reporting programme for healthcare scientists began as a pilot programme in 2012 and is now established as a formal RCPath/IBMS qualification. The qualification is set at FRCPath part 2 level, albeit covering a narrower scope of practice, which is currently either in gastrointestinal, gynaecological or dermatopathological histopathology. Consultant scientist posts are becoming established in a number of laboratories, with many departments, regions and countries looking to following this new training pathway, especially in light of the known workforce shortages in histopathology in the UK, with an increase in workload and not enough histopathologists in the system to meet demand. This article describes some key information relating to the development of scientists through the programme, as well as the benefits to both departments and patients that comes from training scientists and creating consultant scientist posts on completion of training.

Experience and qualifications prior to the programme

Scientists completing the reporting programme in either gastrointestinal, gynaecological or dermatopathological histopathology, undertake a four-stage programme with examinations at Stage A and C, plus a portfolio at each stage. Scientists beginning reporting training must have five years of post-registration experience and by this point will usually have an MSc and additional post-registration qualifications, e.g. the IBMS/RCPath Diploma of Expert Practice in histological dissection (see Table 1).



Developing clinical knowledge

At the start of training, scientific training may have a different emphasis to medical training. While scientists have wide experience in laboratory management, governance and quality, it is likely that they will have had less exposure to clinical situations. Like any medical trainee, scientist trainees also have an educational supervisor and clinical supervisors. The role of the educational and clinical supervisors is to ensure that appropriate training takes place, tailored to the individual needs of the trainee. For scientists, an important route into such training is through integration into the multidisciplinary teams (MDTs) in the relevant area of training. This can lead to training sessions with clinicians in outpatient clinics, endoscopy/colposcopy/dermatology sessions and theatre lists, in addition to personal study based on individual cases.

The exam process

The exam-setting process for scientist trainees is undertaken by qualified RCPath examiners. The Year 1 OSPE for medical histopathology trainees and the Stage A examination for scientists are identical in terms of format and marking processes. The final examination for medical trainees

and the Stage C Examination for scientists differ in only two ways. The scientists' examination is site specific (gastrointestinal, gynaecological or dermatopathology), and scientists are not examined in cytopathology or frozen section reporting. When possible, the same questions are used for both scientist trainees and medical trainees. College examiners are used interchangeably for the examinations and all the short cases are marked at the RCPath central marking day.

In addition to the set examinations the scientists have to produce extensive portfolios that itemise their practice for Stages A, B, C and D of their training. After successfully passing the Stage C exam, scientist trainees are awarded the Advanced Specialist Diploma (ASD) in histopathology reporting by the IBMS. Stage D for scientists mirrors the process for medics, where independent practice is developed. This is done using a "stepping stone" method, following the national RCPath/IBMS document, which sets out guidance for this final stage. After successful completion of Stage D, trainees receive their Certificate of Completion of Training (CCT) and are invited to the RCPath New Fellows Ceremony.

The benefits of having reporting scientists

The introduction of reporting scientists into histopathology teams can provide many benefits. The role of the consultant scientist is different to that of the consultant pathologist. Primarily, consultant scientists are experts in a specific field that can contribute to delivery of a safe diagnostic histopathology service. As consultant scientists have a wealth of experience, they may also have other roles, which contribute to delivery and development of services, both within pathology, but also within wider trust roles. Examples may include laboratory management, clinical governance, UKAS assessment, teaching, research and innovation.

TABLE 1. STAGES OF TRAINING FROM UNDERGRADUATE TO POSTGRADUATE FOR SCIENTISTS AND MEDICS

Year of training	Scientific pathway	Medical pathway
1	Undergraduate degree	Undergraduate degree
2	Undergraduate degree	Undergraduate degree
3	Undergraduate degree	Undergraduate degree
4	HCPC registration *NSHCS Scientist Training Programme MSc/Specialist Portfolio Member/Fellow of IBMS IBMS Diploma of Expert Practice in Histological Dissection	Undergraduate degree
5		Undergraduate degree
6		Foundation Year 1
7		Foundation Year 2
8		ST 1 (OSPE exam)
9	Healthcare Scientist reporting programme	ST 2 FRCPath part 1 exam
10	Stage A Portfolio and OSPE exam	ST 3
11	Stage B Portfolio	ST 4 Final FRCPath exam
12	Stage C FRCPath-equivalent exam	ST 5 Entry to Specialist Register
13	Stage D Consolidation and portfolio	
14	Consultant Healthcare Scientist	Consultant Pathologist

*Optional pathway, which includes MSc study

"Scientists can add value by providing connection and understanding between the laboratory and the clinical team"

IMAGES: GETTY/ISTOCK

With experience in laboratory management and accreditation processes, the practice of scientists is guideline- and protocol-driven. This is of benefit to the histopathology team, as scientists encourage adherence to protocols on specimen description, sampling and reporting. As a result, scientists are in a good position to teach medical histopathology trainees on specimen dissection, block selection and adherence to guidelines and protocols. As well as supporting teaching and training, consultant scientists can release time for consultant pathologists to deliver their other roles, e.g. clinical lead, medical examiner and UKAS assessment.

Responsibility and indemnity

To practice as a healthcare scientist in histopathology, scientists must be appropriately qualified and registered with the Health and Care Professions Council (equivalent body to the GMC for doctors), as a biomedical scientist and/or a clinical scientist. The HCPC regulates both biomedical scientists and clinical scientists, who undergo a revalidation process every two years. All healthcare scientists in the NHS undergo regular appraisal. Consultant scientists are expected to participate in appropriate EQA schemes and will be members of the RCPath or IBMS CPD schemes.

Healthcare scientists have indemnity cover from their NHS employer, and also from the IBMS professional indemnity scheme, if they are members of the Institute. Indemnity covers healthcare scientists to work within their scope of expertise and qualifications and, therefore, scientists are able to work independently at consultant level, taking full responsibility for histopathology cases.

Complexity of work

Consultant scientists are qualified to report the entire spectrum of the curriculum within their scope of practice, ranging from the most simple to the most complex specimens. Although they are able to work independently, they function as part of the specialty team, dissecting and reporting cases within their scope of practice in accordance with service needs.

The diagnostic difficulty of a particular specimen is not determined by its geographical or anatomical source, but by the pathological findings once it is examined. The important factor is knowing one's boundaries of practice and competence and to know when to seek help from colleagues by showing each other cases. This good clinical practice applies equally to consultant scientists and consultant histopathologists.

CREATING POSTS

Consultant scientist posts are beginning to be created around the UK. This will allow full integration into the specialty team and the MDT, while also demonstrating and rewarding the value that the scientist provides to service delivery and facilitating reporting of cases within the national screening programmes. These posts may be completely focused on dissection and reporting, however, they may also include other roles and responsibilities. Model job descriptions for consultant scientists working in histopathology are available on the RCPath website, along with medical histopathologist templates.

The scientist histopathology reporting programme is providing additional staff who can contribute to clinical service delivery. To develop a workforce fit to deal with pressures, it is important that the programme continues to develop. This will be best achieved by having a clear, funded training programme, achieved by collaboration among educational organisations, professional bodies and commissioners.

Reporting screening programme cases

Consultant scientists are able to independently report cases from screening programmes, provided they are in a substantive consultant post. There is a long history of scientists reporting specimens from the NHS Cervical Screening Programme and it is due to changes in this programme that many advanced practitioners in cervical screening are joining the reporting programme for gynaecological pathology. Reporting in the NHS screening programmes is regulated and driven by protocols and guidelines, putting scientists in a good position to report such specimens.

MDT contribution

Consultant scientists are a valuable part of the specialty MDT. During training, attending and integrating into MDTs is a valuable way of increasing clinical knowledge and also building professional relationships and networks. Scientists, together with nurses, physicians, surgeons, oncologists, pathologists, dietitians, psychologists, MDT coordinators and other professionals can be valuable members and contributors to patient care.

The important attributes of team members are to have appropriate training, knowledge and experience. Scientists can add value by providing connection and understanding between the laboratory and the clinical team, due to their wealth of experience within the laboratory setting. Scientists are in a good position to not only give advice to the MDT on cases reported, but also to advise on laboratory aspects and any further testing that may be required. IBMS

Dr Joanne Horne and **Dr Bryan Green** work in cellular pathology at University Hospital Southampton NHS Foundation Trust.

"I see quite a number of other LGBTQ people throughout pathology and it heartens me to see them accepted"

IMAGES: ISTOCK/GETTY

LGBTQ INCLUSIVITY: FACT OR FICTION?

Colin Mudd looks back over the last 40 years in this personal account of LGBTQ issues within the NHS and pathology workforce.

I was delighted to be asked to write about my experience of the inclusivity in our profession of LGBTQ people. The fact that it coincides with LGBTQ History Month resonates particularly with me, as I have had the pleasure of working as a biomedical scientist for over 40 years (44 years, to be precise, on 4 October this year).

As an "old fossil" that has only ever worked at a single trust for all of these years, I can look back over the decades and see how things have changed and, in my view, improved.

This article represents my personal journey and opinions expressed are mine alone. I have had some input from colleagues around the country and thank them for sharing their thoughts and experiences with me.

Secretive and covert

For me, society in the mid-1970s was a very different place compared with today. Being a gay teenager was not the easiest thing in those days; one had to be secretive and covert in so many aspects of life. Fortunately, I have had very few significant negative experiences. However, those that I have had were fairly major.

I vividly recall in the late 70s being "queer bashed" and having to explain it away as a mugging. Equally, I recall with sadness being asked to leave a church that I had regularly attended as apparently I was a "divisive influence". It was quite obvious what the real reason was.

I became reacquainted with one of the people from that church a few years ago and was told that everyone was so surprised I had stopped attending

– they were never told the reason. Add to that of course name calling and other forms of verbal abuse, but over the years one learns to live with it. However, from my experience, this form of abuse has become far less popular. Of course, it very much depends on the society one mixes with.

Acceptance in the profession

In the laboratory, my first manager was very kind and generous to me and, in fact, I came out to him before my own family. Typically, his reply was "that's no surprise, I knew already and just wanted you to tell me". He was tremendously supportive for me coming out to my parents.

Professionally, I have encountered very little negativity, although I did hear that a consultant from another department was playing golf with my manager one day and he commented "you've got one of them in your department haven't you?" Other than that, very little was said directly to me. I recall being described as "flamboyant" – perhaps an alternative term for being gay in the 70s and 80s.

Now as a self-confessed and proud "Old Queen" I feel completely at home. I see quite a number of other LGBTQ people throughout pathology, which heartens me when I visit other laboratories around the country and see the diversity throughout our profession.

Some hospitals are particularly enthusiastic about LGBTQ issues and this can make a great atmosphere and a diverse workforce. However, a friend of mine struggled in their workplace and was accused of trying to "gay" the department by employing LGBTQ people. They were also victim to the ignorance of people regarding AIDS in the 1980s – colleagues would leave the tearoom as he entered (assuming that all gay men were a risk).

I also recall colleagues refusing to perform a manual test on an HIV-positive sample, saying "I'm not putting myself at risk, it's their fault – they deserve it".

"Being LGBTQ should be as mundane as having brown or blonde or (in my case) grey hair"

So, while it hasn't always been an easy or pleasurable journey my experiences over the last 15 to 20 years have been particularly uneventful, which is a truly good thing. Working in an environment where you can feel completely at ease makes for a much happier, comfortable atmosphere and, of course, a much more effective team.

Tolerance and acceptance

So, what is the way forward? Where do we go from here and how do we improve our situation? Perhaps the responsibility lies with us all. The majority of us work for the NHS, where inclusivity should be inherent in the culture and part of a trust's policy. That said, I am sure there are many people out there with much more unpleasant stories to tell. Being in a professional environment with educated people does not preclude ignorance.

I do wonder what it must be like for our transgender friends and colleagues at other hospital laboratories. They have such a difficult time both from a personal perspective and, I imagine, professionally. In a hospital environment I only personally know two transgender people, both of whom are completely accepted by their colleagues. So perhaps I might add a little more to the tolerance and acceptance idea, that we should be open and honest with one another.

Long journey

I am particularly averse to the idea of "gay rights". I do not underestimate the struggle that some people have undertaken to get us to the point in our history. But it seems like a political statement to say that LGBTQ people deserve the same human rights as everyone else. Are we special cases? I love the idea that some people have said that they don't know any gay people. Of course they do... But not everyone needs to wear a rainbow, a pink triangle or be flamboyant to be part of our community. Being LGBTQ should be as mundane as having brown or blonde or (in my case) grey hair.

In response to the question – LGBTQ inclusivity: fact or fiction? – from my experience, we as a profession are tolerant and inclusive. But the journey is a long one and we are not yet at the end. BMS

Colin Mudd is a Higher Specialist Biomedical Scientist at Nottingham University Hospitals NHS Trust.

For LGBT+ History Month the IBMS is looking for members' contributions, which will run as a series of blogs on the website. For more details, contact **communications@ibms.org**

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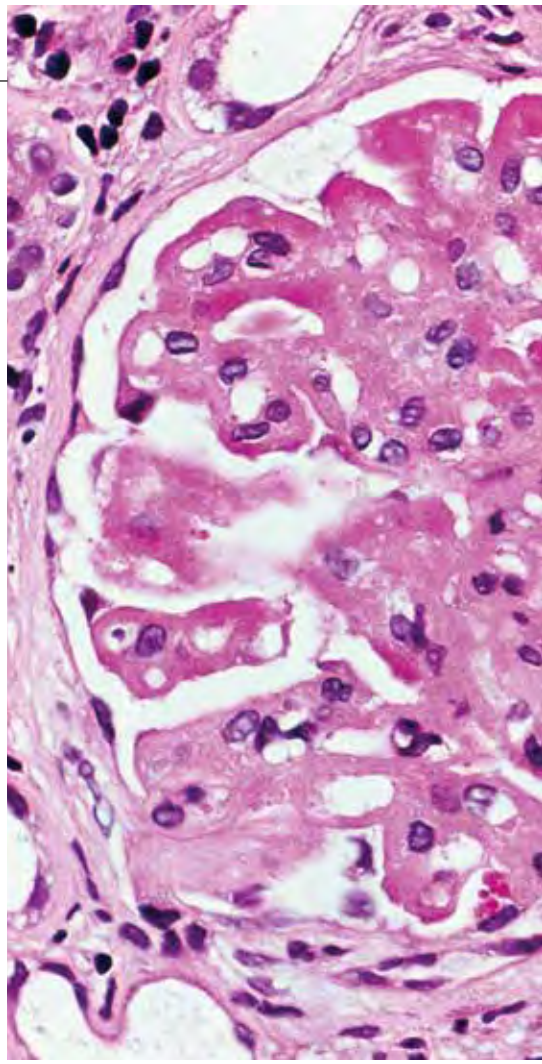


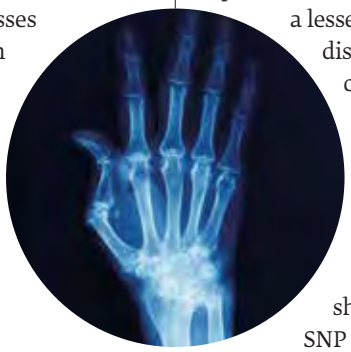
BRITISH JOURNAL OF BIOMEDICAL SCIENCE

ISSUE 1 2020 – SYNOPSIS

Deputy Editor **Tony Rhodes** provides a brief glimpse of the articles on offer in the first issue of 2020.

Firstly, in his editorial to this issue Editor Andrew Blann provides a review of what we have learnt from the articles published in the journal in 2019. The editorial is useful reading for those wishing to publish, as it captures the essence of what the journal is about and provides an excellent overview of the type of article and subject material published so far. No doubt it will also be a valuable point of reference for those of us undertaking journal-based learning as part of our continuing professional development.

Single Nucleotide Polymorphisms (SNPs) and/or microRNA (miRNA) and their pathological associations feature in many of the articles published in this issue of the journal (Gupta et al, Bahreini et al, Ramezani et al, Tian et al, Adbulla et al), whilst two of the articles involve autoimmune disease processes in glomerulonephritis (Tian et al) and rheumatoid arthritis (RA) (Huang et al). In addition, a total of four of the studies published in this issue focus on epithelial cancers (Gupta et al, Bahreini et al, Ramezani et al, El-Bendary et al).



SNP, miRNA and cancer

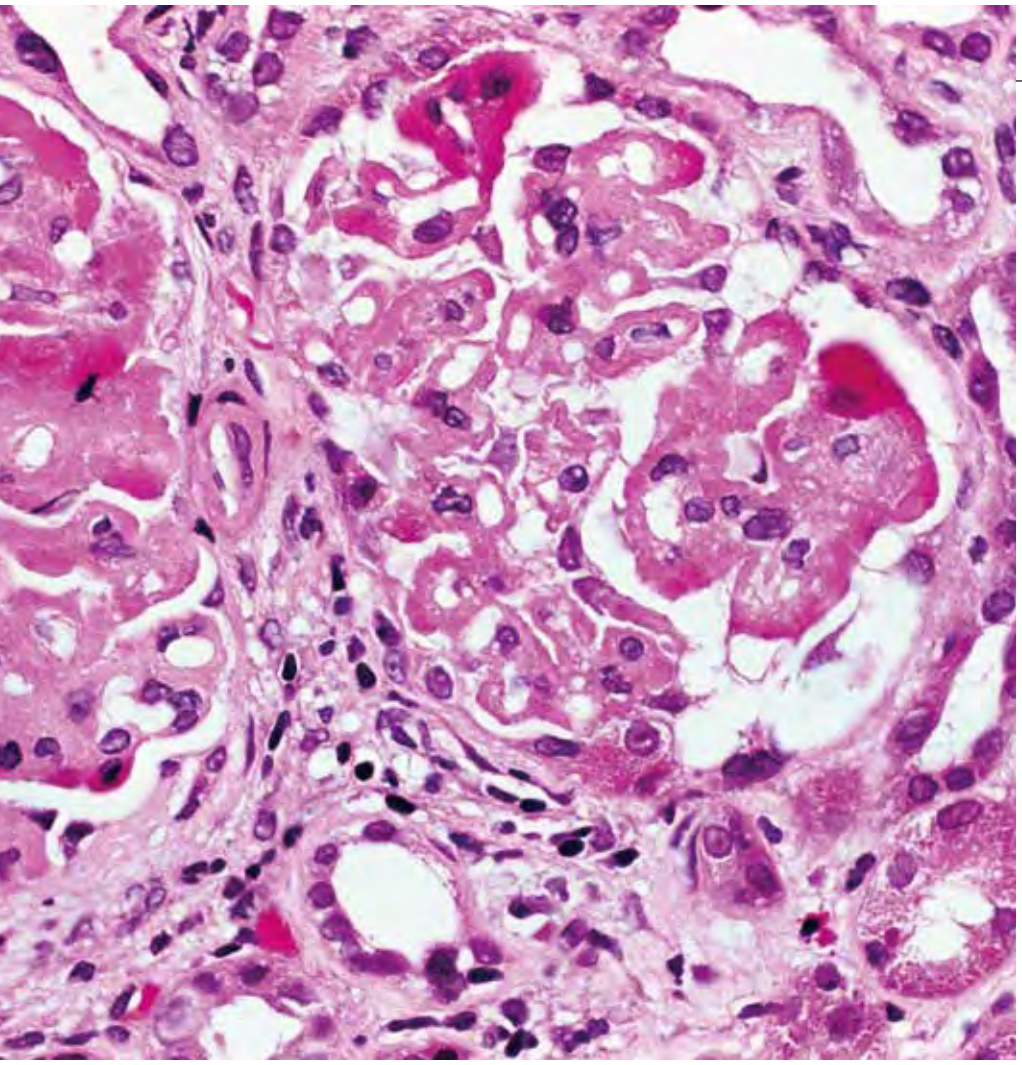
Gupta et al show that polymorphisms in the XRCC4 gene responsible for DNA repair are associated with cervical cancer, Bahreini et al show how a polymorphism in the mi-RNA-559, rs5840758, is linked to breast cancer, whilst Ramezani et al investigate how circulating miRNA can be used as a blood-based marker of breast cancer, showing the differential expression of the circulating miRNA, with -miR-125a-3P decreasing and -miR–125b levels increasing in the disease, respectively.

Autoimmune disease processes in glomerulonephritis and rheumatoid arthritis

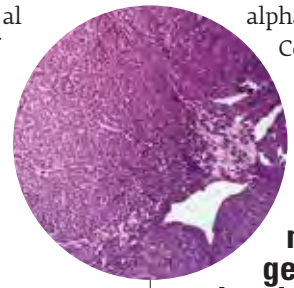
Membranous nephropathy (MN), the underlying disease process responsible for the nephrotic syndrome in adults, is predominantly idiopathic (IMN), and to a lesser degree secondary to other diseases (SMN). IMN is now considered by many to be an autoimmune disease, in which autoantibodies target the M-type phospholipase A2 receptor (PLA2R) on glomerular podocytes. Recent studies show an association between SNP of PLA2R1, and in this issue of the journal Tian et al investigate the expression of five of these SNP in Chinese patients with IMN and SMN.

RA is a chronic and systemic autoimmune disease in which there is destruction of synovial tissue of the joints due to a chronic inflammatory process, resulting in loss of joint function. Whilst the exact pathogenesis of RA has yet to be established, cytokines and inflammatory mediators play a key role. The 14-3-3 family of proteins, which have a range of functions, to include involvement in inflammation, are known to be important in the development of RA, with serum 14-3-3η upregulating cytokines and allowing systemic inflammation to persist. Recently the protein has become used clinically as a marker for the disease in addition to existing markers, such as anticitrullinated peptide antibodies (ACPAs) and the rheumatoid factor (RF).

In addition, the pro-inflammatory cytokine, high mobility group box-1 (HMGB1) plays a role in the pathogenesis of many diseases, including RA. In this



issue of the journal, Huang et al set out to determine which of these markers alone or in combination provide the best data for the diagnosis of RA.



Methylation of tumour suppressor genes and E-cadherin in hepatocellular carcinoma

Cancer of the liver (hepatocellular carcinoma) is a leading cause of death in many parts of the world and is frequently associated with long-standing infection with either the hepatitis B virus (HBV) or hepatitis C virus (HCV). In this issue of the *British Journal of Biomedical Science*, El-Bendary et al, investigate the methylation of tumour suppressor genes (RUNX3, RASSF1A) and the cell adhesion molecule, E-cadherin, in HCV related liver cirrhosis and hepatocellular carcinoma. They report the methylation status of the E-cadherin gene to be an independent risk factor for cases of HCV-associated hepatocellular carcinomas with low alpha-fetoprotein (AFP). Consequently, this finding may be of diagnostic value in such cases.

SNP for collagen and metalloproteinase genes and their involvement in keratoconus

Keratoconus, a corneal disease typified by thinning of the cornea and resulting in irregular astigmatism and decreased vision, may be linked to a decreased amount of total collagen matrix. Matrix metalloproteinase-9 (MMP9) and gelatinase are the main matrix-degrading enzymes produced by the corneal epithelium. The balance of MMP9 activity is in turn regulated by tissue inhibitors of matrix metalloproteinase (TIMPs). In their article, Abdullah et al hypothesise that SNP for collagen IV, MMP9 and TIMP-1 genes play a role in the pathogenesis that leads to the corneal thinning seen in keratoconus.

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"If further studies can verify these results, it will increase our understanding of the disease"

Alkaline phosphatase levels and epilepsy

Rawat et al, in their biomedical science in brief, show that the raised alkaline phosphatase (AP) levels frequently seen in patients with epilepsy are related to the frequency of recurring epileptic seizures and how recently they occurred and not due to the metabolic and pharmacological interactions of epileptic drugs, as previously thought. They were able to show this by comparing results in a previously untreated, drug-naive, group of patients compared to a group already receiving medication. If further studies can further verify these results and elucidate the mechanisms involved, it will clearly increase our understanding of the disease.

Case study of Madelung disease

Hoxha et al from Tirane, Albania, present a case of Madelung disease; an extremely rare condition with an incidence of just 1/250,000 and occurring more commonly in the Mediterranean populations. It is characterised by symmetrical abnormal growth of adipose tissue, occurring particularly around the neck, upper limbs and chest. The main differential diagnosis is Cushing's syndrome, which was ruled out following laboratory tests for cortisol levels. In this case report, the authors summarise what is known about the disease and the investigations taken to arrive at the definitive diagnosis.

CPD

Any of the above may be the subject of Journal-based learning. BMS

MY IBMS NEWS

PROFESSIONAL ACHIEVEMENT

IBMS SPONSORS AHA AWARD

This year, the IBMS is again sponsoring the Advancing Healthcare Awards (AHA) award for Biomedical Scientist of the Year.

The award celebrates an exceptional biomedical scientist who has used 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.

Entries have now closed, with the judging day taking place on 13 February and the awards ceremony to be held on 20 March.

Awards are judged by looking at measurable achievement, leadership and teamworking and impact on patient care.

Last year's winner of the Biomedical Scientist of the Year award was IBMS fellow Jo Horne.

After winning, she said: "I was thrilled to be nominated and shortlisted for the Biomedical Scientist of the Year award, alongside other fantastic biomedical scientists from around the UK. Receiving this recognition from my peers was incredible enough, but to then go on and win the award was one of the proudest moments of my professional life.

"To be recognised by my peers is amazing, and I only hope that I can inspire others working in biomedical science to set the bar high, achieve their own goals and then encourage others to do the same."

→ For more information on the awards, visit the website ahpandhsawards.co.uk

MEMBER ISSUES

IBMS position statements

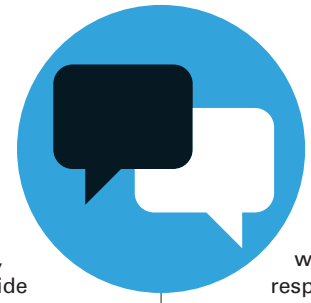
The IBMS is open to hearing and addressing our members' issues and representing the profession's interests across the four nations, and beyond.

Members are being invited to raise topics for IBMS position statements and opinion pieces.

For a topic to merit the production of a position statement or opinion piece, it must be of significance to a majority of the membership or, exceptionally, to a single discipline or professional group within the membership, and be a key issue for the Institute.

Suggestions for topics and the rationale behind the suggestion should be sent by email to communications@ibms.org and entitled "IBMS Position Statement".

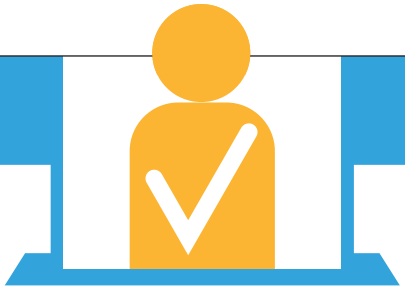
It will then be forwarded to IBMS Chief Executive Jill Rodney and the appropriate IBMS Council members, who will then decide upon the suitability of the proposal within five working days.



In the event that a proposal is accepted, a suitable lead author will be appointed, usually from the IBMS Council, panels or staff.

The lead author will have 14 days to respond and then send their statement/piece to Council for approval.

Unless revisions are requested, the statement will be published within a further five working days.



COUNCIL ELECTIONS: YOUR CHANCE TO SHAPE THE FUTURE OF THE IBMS

The IBMS prides itself on being a professional body that is run by its members for its members. It is currently looking for corporate members who will use their professional knowledge, leadership skills and experience to set the strategic direction of the Institute, shaping its future and ensuring it continues to meet its members' needs.

The role of a Council member is hugely rewarding but requires significant personal commitment and skills, strategic thinking, financial understanding, passion for the work of the Institute and the ability to be a role model for the profession. Council members are leaders of the profession and candidates should ideally be active in the profession at the time of standing for election.

Nominations for corporate members to participate in the 2020 elections to Council are now invited, as there are vacancies for two National and two Regional members as follows:

NATIONAL MEMBERS

Two vacancies - three-year term

REGIONAL MEMBERS

Two vacancies - three-year term

- South East
- Wales

Find out more about becoming an IBMS Council member and fill in the online application form at www.ibms.org/elections

Deadline for return of nomination forms: 5.00 pm on Thursday 5th March 2020.

MEMBER BENEFITS

IBMS DIARY OPT-OUT

There is now an option to opt out of receiving the IBMS Diary from 2021.

In these digital times, when people are more aware of their environmental impact than ever, the IBMS has decided to add an option to opt out of receiving the IBMS Diary.

Those who do not wish to receive the diary should update their IBMS preferences. Those who do so will not receive a diary in the October 2020 edition of *the Biomedical Scientist* (or future editions).

→ **bit.ly/2sHOdyR**

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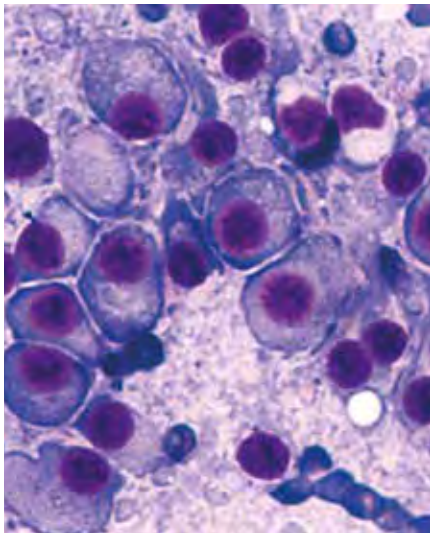

BIRMINGHAM CPD

MYELOMA PRESENTATION

A CPD presentation entitled "UK Myeloma Trials: Major advances in diagnosis and management" is taking place in Birmingham.

Professor Mark Drayson, Director of the Clinical Immunology Service at University of Birmingham, will deliver the presentation on 12 February.

It will take place at the Seminar Room in the Education Resource Centre at Birmingham Women's Hospital.

A buffet will be served from 5.30pm, the presentation will start at 6.30pm and all IBMS members are welcome.

→ **For further details and to confirm attendance, please contact Nigel Coles on nigel.coles@nhs.net or 0121 335 8034 by 5 February.**

PODCASTS

NEW PODCASTS NOW

Episode three of the new series of IBMS podcasts is available to listen to online now.

It features Professor Barbara Bain discussing her research and issues around morphology.

A new molecular pathology podcast is also due to go live on the IBMS website any day now.

With self-directed learning becoming increasingly important for staying up to date with the latest research and news and developing knowledge for the wide range of IBMS exams, the podcast is aimed to be a valuable learning and CPD resource for members.

→ **To access the podcast and listen to previous episodes, visit ibms.org/resources/podcasts**

CELEBRATING SUCCESS IN 2019

Chris Ward, IBMS Head of Examinations, celebrates some of the achievements of members who have obtained Institute qualifications in the last year.

Near the start of each year we rightly take a moment to reflect and celebrate the achievements of some of the members who have obtained various IBMS qualifications in the preceding year. The candidates shown opposite passed the specified higher qualifications, however, we would also like to congratulate everyone who passed an IBMS qualification in 2019. In addition to the names stated here, over 1000 gained their Certificate of Competence and just over 400 passed the Specialist Diploma in their chosen discipline. A total of 175 were successful in achieving the Certificate of Expert Practice (CEP) in Leadership and Management, Quality Management, Molecular Pathology or Training.

Feedback from successful candidates shows that there is clear evidence that the achievement of an IBMS qualification helps to facilitate professional and career development opportunities. In these times of continued financial constraint, they provide value for money by helping to allow organisations to support their staff at all levels with qualifications that are specifically designed for those who are working in laboratory settings. They provide an affordable and specialist alternative to academic qualifications.

It is essential that we continue to develop staff because they are the future leaders of this profession and our

qualifications encourage critical thinking, questioning attitudes, reflective practice and the development of greater autonomy, all of which are essential skills for leaders. They are both developed and assessed by IBMS expert practitioners and academics from IBMS-accredited universities in collaboration with, where appropriate, colleagues from the Royal College of Pathologists (RCPath).

They represent a considerable commitment of both time and effort by the individual concerned. Those who pass will have demonstrated to the examiners a comprehensive understanding of complex scientific, technical and managerial subjects and that they can apply their knowledge, competence, personal autonomy, as well as transferable skills and qualities, in their chosen discipline. Those who have been successful will find that their new qualification provides both peer and wider professional recognition.

Successful achievement of the Specialist Diploma allows individuals to upgrade to Member (MIBMS) status, while success in the Higher Specialist Diploma (HSD), the Advanced Specialist Diploma (ASD) in Histopathology Reporting, or the ASD in Specimen Dissection, or Non-Gynaecological Cytology, along with the pre-requisite Diploma of Expert Practice (DEP) qualifications, provide eligibility for upgrade to the highest level of IBMS membership – Fellowship (FIBMS) status.

Many of those who sit on one of the eight IBMS Specialist Advisory Panels have previously achieved at least one of these qualifications. Panel members play a crucial role in supporting the work of the IBMS through their contributions to the review of IBMS qualifications (such as the HSD Review that I wrote about in the October and November editions of *the Biomedical Scientist* last year), the development of professional guidance and responding to consultations. The advisory panels are also responsible for the development of the Congress scientific programmes and planning for Congress 2021 will start in a matter of weeks.

Congratulations to all those who passed an IBMS qualification in the last year and best of luck to those undertaking one this year.

EXAMINATION PASS LIST 2019

The following members were successful in Institute examinations during 2019.

Higher Specialist Diploma

Cellular Pathology

Maria Cunningham - Craigavon Area Hospital
Jemma Morris - Calderdale Royal Hospital
Vida Motamedi - Royal Gwent Hospital
Ricky Thomas - Calderdale Royal Hospital

Clinical Chemistry

Charlotte Atkin - Diana Princess of Wales, Grimsby
Gareth Blackburn - Royal Lancaster Infirmary
Jennifer Kettlewell - Scarborough General Hospital
Mildred Tan - Royal Marsden Hospital
Catherine Wisher - Diana Princess of Wales, Grimsby

Cytopathology

Donna Morrison - Aberdeen Royal Infirmary
Yamuna Sujith - King's College Hospital NHS FT

Haematology

Carly Batson - Macclesfield Hospital
Hayley Trigwell - Queen Elizabeth University Hospital, Glasgow

Immunology

Faye Sims - Peterborough City Hospital

Leadership and Management

Musfira Bukht - Great Ormond Street Hospital

Medical Microbiology

Philip Black - Craigavon Area Hospital
Rachel Dyson - Queen Elizabeth Hospital, Gateshead
Martine Jensen - Hull Royal Infirmary

Transfusion Science

Michelle Evans - Newcastle upon Tyne Hospital's NHS FT
Jessica Jones - University Hospital, Birmingham
Kenzi Potter - Antrim Area Hospital

Diploma of Specialist Practice

Mary Busby - University Hospital, Llandough

Certificate of Expert Practice

Flow Cytometry

Emma Stansfield - Manchester University NHS FT

Diploma of Expert Practice

Histological Dissection

Claire Barber - King's Mill Hospital (Sutton-in-Ashfield)
David Bean - St. George's Hospital, Tooting
Aneliese Bennett - Dewsbury & District Hospital
Katherine Carlsson - North Tyneside General Hospital
Steven Clarke - Worcestershire Royal Hospital
Philip Gibson - North Tyneside General Hospital
Ashley Gilchrist - The Royal Marsden Hospital
Joanne Grindle - Manchester University NHS FT
Michael Ho-Kan - The Royal Free Hospital
Michelle Howlett - Ipswich Hospital
Leanne Hughes - Cheltenham General Hospital
Robert Lees - St. George's Hospital, Tooting
Morgan Long - St. George's Hospital, Tooting
Rajesh Nalluri - Northwick Park Hospital
Julie O'Brien - Royal Oldham Hospital
Emily Potter - Mid Yorkshire Hospitals
Matthew Potter St James's University Hospital, Leeds
Colleen Smith - Singleton Hospital, Swansea
Hayley Spencer - Nuffield Health Tunbridge Wells
Damneet Thind - Health Services Laboratories

Immunocytochemistry

Victoria Barnwell - John Radcliffe Hospital, Oxford

Non-Gynaecological Cytology

Anna Chan - Royal Derby Hospital
Jane Dickinson - Queen Elizabeth Hospital, Gateshead
Jane Girgis - New Cross Hospital, Wolverhampton
Trevor Jones - Singleton Hospital, Swansea
Melissa Ellis - Wycombe Hospital

Advanced Specialist Diploma

Cervical Cytology

Francesca Albertini - Ashford and St Peter's Hospital, Chertsey, Surrey

Specimen Dissection – Urology

Gavin Regan - Royal Derby Hospital

Histopathology Reporting

Lindsey Dixon - Royal Sussex County Hospital
Dafydd Eilir Jones - Swansea Bay University Health Board
Rachel Puw Jones - Royal Gwent Hospital, Gwent

JOURNAL-BASED LEARNING EXERCISES

Institute of Biomedical Science Continuing Professional Development

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

DEADLINE WEDNESDAY 6 MAY 2020

Next-generation protein analysis in the pathology department. Ahmed M, Broeckx G, Baggerman G *et al. J Clin Pathol* 2020; **73** (1): 1–6. https://jcp.bmj.com/content/73/1/1 Assessment No: 020720

01	Traditionally, immunohistochemistry (IHC) is used by pathologists to localise specific proteins or peptides in tissue sections.	11	In mass spectrometry, a laser beam irradiates the matrix.
02	Measurement of protein alterations fails to predict functional consequences (and thus diagnosis and prognosis) any better than DNA alterations.	12	MALDI is typically coupled to a time of flight (TOF) mass analyser.
03	MALDI IMS stands for matrix-assisted laser desorption/ ionisation imaging mass spectrometry.	13	The mass range in a normal MALDI-TOF instrument is limited and usually amounts to 30 kDa.
04	The essence of IHC is to make specific proteins or peptides visible under the microscope by means of antigen-antibody recognition by a specific immunoglobulin or primary antibody.	14	In MALDI IMS the mass spectra are recorded with their two-dimensional coordinates on the tissue slide.
05	Monoclonal antibodies have better sensitivity, while polyclonal antibodies tend to be more specific but less sensitive and give more background staining.	15	MALDI is not a soft ionisation process because the matrix is the actual energy absorber.
06	IHC neither helps to subtype tumours, nor visualise specific structures within tissues.	16	There have been publications highlighting the use of MALDI IMS in lung cancer, breast cancer, gastrointestinal tract cancer among others.
07	Evaluated predictive factors in IHC include evaluation of ALK translocation in lung, and V600E mutation status in malignant melanoma.	17	The MALDI IMS method is not suitable for the detection of human papillomavirus.
08	Mass spectrometry encompasses a whole set of techniques to analyse different molecules, limited to proteins and peptides based on the molecular mass.	18	When comparing the techniques used for IHC and MALDI imaging, tissues are generally thicker for MALDI imaging.
09	An additional preparation step required for high-molecular weight proteins is trypsin.	19	A huge advantage of MALDI imaging over IHC is that more than 100 peptides can be evaluated at once.
10	High molecular weight proteins are easily detected in MALDI analysis.	20	In the TagMass method, a specifically designed antibody against a target antigen is linked to a laser-cleavable peptide with a known sequence.

REFLECTIVE LEARNING

01	Critically review the quantitative use of immunohistochemistry in your laboratory.	02	Critically review the prognostic and predictive testing which occurs on patient samples within your laboratory.

DEADLINE WEDNESDAY 6 MAY 2020

Transfusion requirement and length of stay of anaemic surgical patients associated with a patient blood management service: a single-centre retrospective study. Faulds J, Whately-Smith C, Clarke K. *Transfus Med* 2019; **29** (5): 311–8. Assessment No: 020220

01	A pre-operative haemoglobin of <120 g/L has been associated with a 10-fold increase in the requirement for allogeneic blood transfusion following total hip and knee joint arthroplasty.	**11**	The surgery database included 26,641 separate records and the PBM database comprised 1910 records.
02	Since 2003, patient blood management (PBM) includes all surgical specialties, supporting both primary and secondary care.	**12**	For patients with multiple surgeries in the year, data were collected from all surgeries.
03	Oral iron is well tolerated and the effects are instant.	**13**	Overall, 3% of patients were transfused and, of these, 83.3% of transfusions occurred in patients who had been identified as anaemic.
04	In 2015, Kotze *et al*. found that a full treatment dose of intravenous (IV) iron can be given rapidly, generally without side-effects, with a rapid increase in blood values after 2–4 weeks.	**14**	Overall, the length of stay for PBM and non-PBM patients was 3.7 and 2.1 days, respectively.
05	As part of the PBM programme, pre-operative anaemia assessment and correction began in orthopaedics in 2006 and was expanded to all surgeries in 2009.	**15**	Within Table 1, both PBM and non-PBM anaemic groups show that there were more females than males.
06	Once patients are accepted and added to an elective surgery list, GPs are asked to perform baseline blood tests that include full blood count (FBC), C-reactive protein (CRP) and reticulocyte count.	**16**	Table 2 shows that the highest percentage of patients who were transfused were anaemic and were assessed by PBM.
07	Patients identified as iron-deficient with or without anaemia (Hb <120 g/L and either ferritin <30 ng/mL and CRP <20 g/L or ferritin <70 ng/mL and CRP >20 g/L) are considered for haemoglobin optimisation.	**17**	Of patients who had been assessed for pre-surgery anaemia correction, 26.7% were initially recommended no iron therapy.
08	Patients undergoing surgery in the calendar month of January 2017 were excluded as they may not have been assessed for anaemia correction in 2017.	**18**	The surgical specialties demonstrate that the largest proportion of anaemic patients not assessed for anaemia correction were those undergoing orthopaedic surgery.
09	The main study outcomes were the requirements for perioperative blood transfusion.	**19**	Length of stay was longer in patients where pre-surgery anaemia had not been assessed.
10	The risk of blood transfusion associated with each procedure was retrospectively designated as high risk, low risk or uncertain, based on the subjective assessment of the procedure.	**20**	Patient blood management activities in Europe and the UK are integrated into routine care pathways for surgical patients.

REFLECTIVE LEARNING

01	Compare and contrast the adverse reactions that can occur with both blood transfusions and IV iron infusions.	**02**	Discuss the benefits of including PBM strategies into pre-assessment pathways and how the blood transfusion laboratory can play a role in this.

EVENTS AND TRAINING COURSES

IBMS Institute of Biomedical Science Continuing Professional Development

More training courses, CPD and local events and activities are available on the IBMS website.

DATE	TITLE	VENUE CONTACT
February		
12 Feb	**CPD presentation: "UK Myeloma Trials: Major advances in diagnosis and management"**	Birmingham I nigel.coles@nhs.net
12 Feb	**UK NEQAS Cellular Pathology Technique Tissue Preparation Techniques Workshop**	Gateshead I cpt@ukneqas.org.uk
13 Feb	**UK NEQAS Cellular Pathology Technique Introduction to Cellular Pathology, Tissue Morphology and Recognition Workshop**	Gateshead I cpt@ukneqas.org.uk
March		
2-3 Mar	**Introduction to Practical HPLC Course**	Rochester I stuart@laserchrom.com
4-5 Mar	**Intermediate Practical HPLC Course**	Rochester I stuart@laserchrom.com
9-11 Mar	**Practical HPLC Method Development Course**	Rochester I stuart@laserchrom.com
12-13 Mar	**Practical HPLC Troubleshooting Course**	Rochester I stuart@laserchrom.com
15-16 Mar	**Practical HPLC Troubleshooting Course**	Rochester I stuart@laserchrom.com
30 Mar-3 Apr	**Microbiology Society Annual Conference 2020**	Edinburgh I conferences@microbiologysociety.org
April		
15 Apr	**UK NEQAS Cellular Pathology Technique Introduction to Immunocytochemistry Workshop**	Northumbria I cpt@ukneqas.org.uk
16 Apr	**UK NEQAS Cellular Pathology Technique Advanced ICC Applications in Laboratory Practice A Workshop**	Northumbria I cpt@ukneqas.org.uk
24 Apr	**Association of Anatomical Pathology Technologists and Human Tissue Authority Consent Training Day 2020**	London I christianburt@ibms.org
May		
6 May	**UK NEQAS Cellular Pathology Technique Non Gyn Cytology Beginners/ Refresher Workshop**	Gateshead I cpt@ukneqas.org.uk
7 May	**UK NEQAS Cellular Pathology Technique Non Gyn Cytology Intermediate Workshop**	Gateshead I cpt@ukneqas.org.uk
20 May	**UK NEQAS Cellular Pathology Technique TEM workshop**	Leicester I cpt@ukneqas.org.uk
June		
10-12 Jun	**The Laboratory Diagnosis of Malaria**	London I claire.rogers@lshtm.ac.uk
15-19 Jun	**The Laboratory Diagnosis of Parasites**	London I claire.rogers@lshtm.ac.uk
17 Jun	**UK NEQAS Cellular Pathology Technique Introduction to Specialist Demonstration Techniques**	Northumbria I cpt@ukneqas.org.uk
18 Jun	**UK NEQAS Cellular Pathology Technique Specialist Demonstration Techniques A**	Northumbria I cpt@ukneqas.org.uk
26 Jun	**Scottish Association of Histotechnology – 43rd Scientific Meeting**	Dunfermline I sah.generic@nhs.net
August		
5 Aug	**UK NEQAS Cellular Pathology Technique Tissue Preparation Techniques Workshop**	Gateshead I cpt@ukneqas.org.uk
6 Aug	**UK NEQAS Cellular Pathology Technique Introduction to Cellular Pathology, Tissue Morphology and Recognition Workshop**	Gateshead I cpt@ukneqas.org.uk

HERE TO HELP

HELP US SUPPORT YOU

Jocelyn Pryce and **Richardia Penn** from the IBMS education team outline how members can help ensure the qualification, registration and training processes go as smoothly as possible.

IMAGES: ISTOCK

Those of you who regularly read this column will know that we are always here to help our service users and members with any queries regarding our qualifications, registration and training.

Last month's article reviewed the successes of 2019 and looked forward to 2020 and, following that, this month seemed perfect timing for us to reflect on how we might help you and how you might help us to do that.

Supporting you is important to us and we do this in numerous ways, including local and national training events, the information on our website and in the form of guidance documentation held there, as well as from our team here at Coldbath Square in London.

Here are some ways that you can help us to help you:

01 If you are planning on applying for a portfolio or verification/examination, please refer to the website for the current version of the application form, as this will help us to process your application faster. Inaccuracies can cause delays.

02 Please ensure that you have filled out all relevant sections on our forms. We have received feedback in the past that the information required on forms was repetitive and we have spent significant time reviewing this, ensuring that we only ask for information that is required. We use each stage as a check-point for information we hold about you and your candidate to ensure that we have correct details.

03 Please regularly refer to the guidance given on our website, as this can change and you may be following an outdated process or using an old form.

Each of the above can slow the internal processes down while we follow up and this can lead to longer turnaround times for you. If you are in doubt, please visit the website or, if you can't find the information you are looking for there, contact the team for advice.

As many of you will know, the length of time it takes to allocate verifiers and examiners is reliant upon them volunteering to undertake the assessments. Delays can be due to numerous reasons, including geographical location and discipline. In order to try to speed the process up, verifiers and examiners may be contacted by one of our team to see if they would be able to undertake an urgent assessment. We would obviously be very appreciative if, when contacted, you are able to help, but don't worry if you can't, we fully understand. If you are not currently a verifier/examiner but would be interested in becoming one, please visit the website for further details, including our training days, or contact registration@ibms.org.

The IBMS education offering will only be successful as long as there is a strong relationship between us and our service users and members and this relationship has never been better. We work hard to respond to your feedback and improve our services wherever we can and we hope that you will continue to help us to help you to be the best! IBMS

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MY LAB

HAEMATOLOGY AND BLOOD TRANSFUSION

Principal Biomedical Scientist **Nicki Lawrence** gives a guided tour of her laboratory at Royal Stoke University Hospital.

Royal Stoke University Hospital (RSUH) is part of the University Hospitals of North Midlands (UHNM) NHS Trust, which covers two sites – Royal Stoke in Stoke-on-Trent and County Hospital in Stafford, and employs around 11,000 members of staff. As a university teaching hospital, we work very closely with our partners at Keele and Staffordshire universities, and we have a patient-centred clinical research facility providing state-of-the-art facilities.

From these hospitals we provide a full range of general acute hospital services for approximately 900,000 people living in and around Staffordshire and beyond. The trust also provides specialised services, cancer services, neonatal and paediatric intensive care and spinal surgery for three million people in a wider area, including neighbouring counties and North Wales. We have one of the busiest emergency departments in the country, with patients being brought to us from a wide geographical area, due to our status as a major trauma centre.

Due to our large population reach and the wide range of routine and specialist services offered by our trust, we run a 365 day, 24/7, ISO 15189-accredited haematology and blood transfusion service. We process in excess of 850,000 FBCs, around 225,000 coagulation samples, and approximately 35,000 blood films per annum. We also have dedicated sections for specialist coagulation investigations, haemoglobinopathy screening, and immunophenotyping for immune monitoring and our peripheral blood autologous stem cell transplant programme. Our blood transfusion department cross-matches over 35,000 units per annum and is kept extremely busy by the trauma centre, cancer centre, maternity unit and our specialist surgical teams, such as cardiothoracic surgery.

We have an excellent team of approximately 70 highly competent, motivated individuals who rotate through both departments, comprising medical laboratory assistants, associate practitioners, trainees and biomedical scientists. Haematology and blood transfusion UHNM is an IBMS-accredited training laboratory and we have a passion for training and education. We have a number of individuals who are currently completing undergraduate and postgraduate studies in biomedical science via a variety of methods, such as day release for apprenticeships, or distance learning for Masters.

As an IBMS-accredited training laboratory we also have members of the team who have completed IBMS qualifications, including the registration portfolio, specialist portfolio, certificates of expert practice in training and quality, higher specialist diploma, and the diploma of expert practice in routine haematology. Offering development opportunities to our team ensures we have a highly knowledgeable workforce who are dedicated to providing a first-class, high-quality service to all of our service users, both within the trust and externally. Our department also has close links to our partner universities, with both clinical and laboratory staff delivering expert lectures on a range of haematology, blood transfusion, and thrombosis and haemostasis topics.

Nicki Lawrence is a Principal Biomedical Scientist and Advanced Practitioner in Morphology working in haematology and blood transfusion at Royal Stoke University Hospital.

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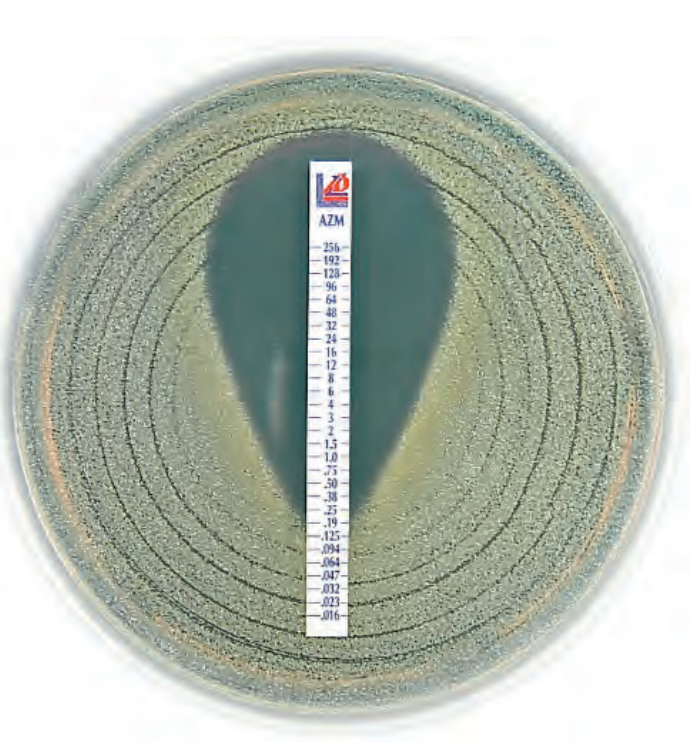

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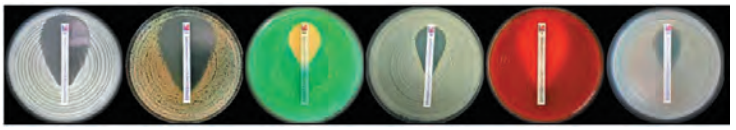

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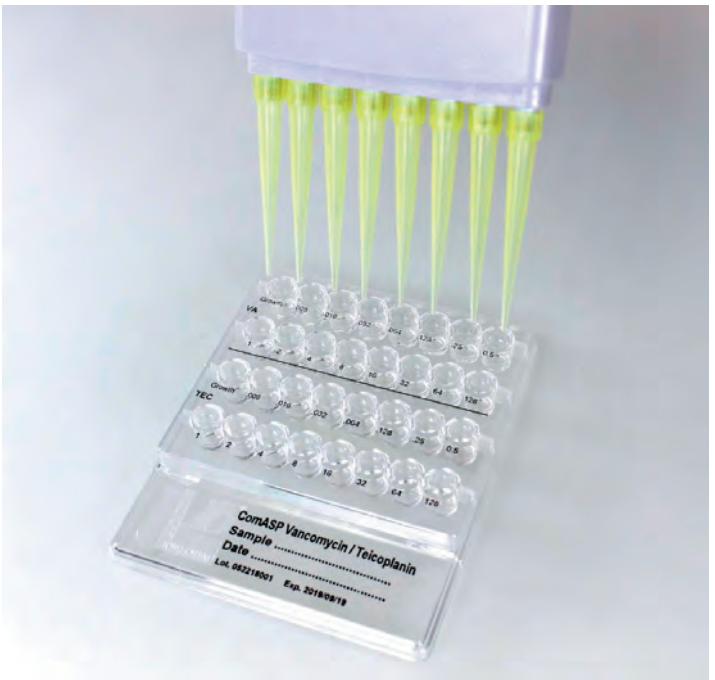

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