THE BIG QUESTION

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ONE-TO-ONE

A NEW ANTIBIOTIC

The latest on the fight against drug-resistant bacteria: *p.16*

HOW TO...

BLOOD STOCKS

Ensuring effective blood stock management: *p.38*

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DECEMBER 2018

FROM PROFESSIONAL TO PATIENT

Three scientists tell their personal stories

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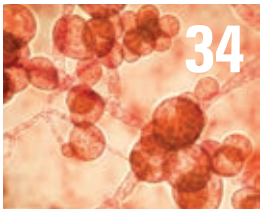

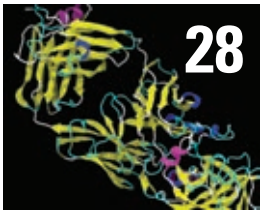

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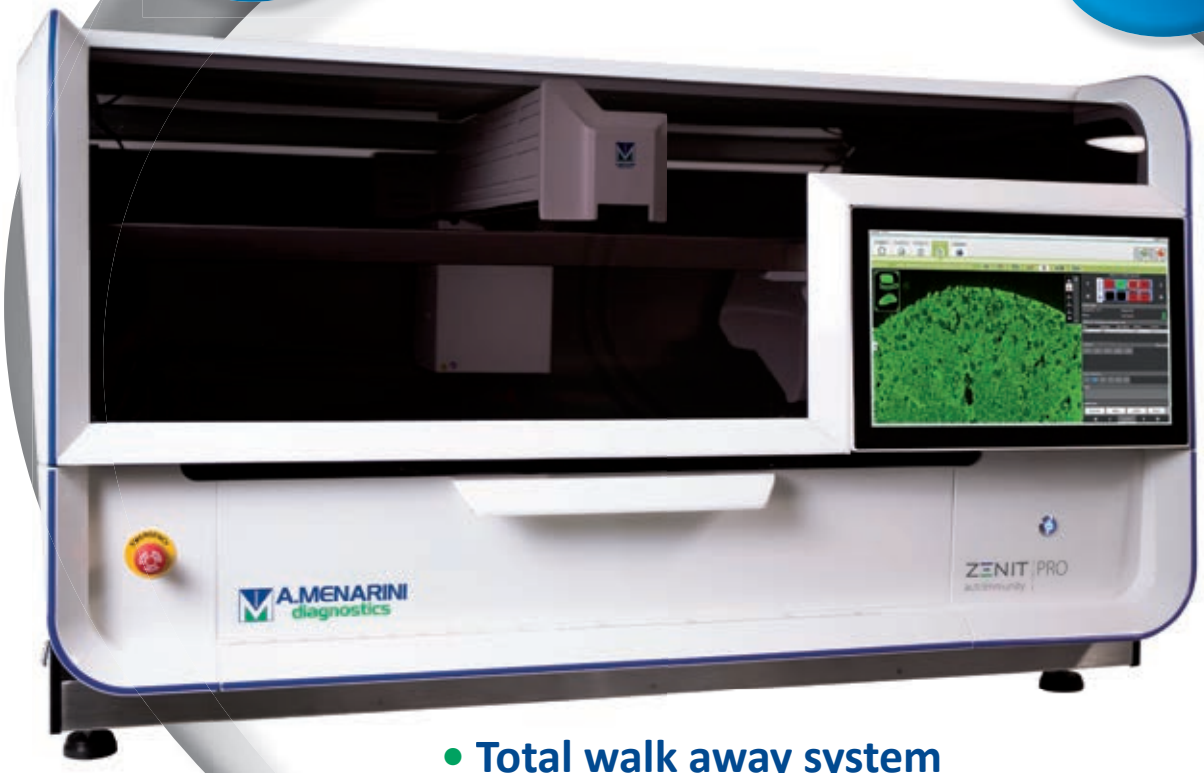

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A WISH FOR CHRISTMAS

This year, Sarah May, IBMS Deputy Chief Executive, is asking Santa for recognition for biomedical scientists.

Dear Santa,

I work for a profession that is populated with dedicated, hardworking people who are generally not having an easy time and who would really benefit from a chance to pause and draw breath and to know they are appreciated for what they do. I've been privileged to share 2018 with some pretty amazing travelling companions and for this reason please can I ask you bring them some very special gifts?

I would like the politicians and service planners to have the wisdom to see the importance of biomedical scientists in healthcare and to see that people would be so much poorer in health without them and for the truth of what happens when a workforce is cut to the minimum to be recognised.

I want our scientists to never doubt the goodness that they do every day they step into a laboratory and I want them to have the strength to carry on doing it, even though it can be tough and often thankless. Please can work be fulfilling, not frustrating and can they have the chance to achieve their aspirations, whatever they may be?

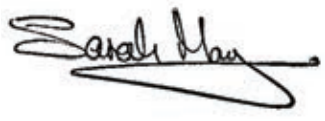
On a more personal level, please can we have the stamina to last the round of seasonal festivities and the grace to know that not all of us can look cool when trying to do "the Floss" on the dance floor. For those brave souls who are still determined, please direct them to the nice YouTube instructional video and remind them to note the age of the very bendy, flexible girl – she's about 15.

For those of us who are planning to cook a turkey on 25 December, please let us have the confidence to believe there is nothing mystical about a large breed of poultry, it just needs a bit longer in the oven, and it doesn't need the wisdom of a celebrity chef to tell us how to make perfect roast potatoes – it's the same as for any other day of the year.

Finally, please can we all have a limitless supply of sense of humour to enable us to appreciate that sequins, inflatable snowmen and Kevin the Carrot are all obligatory parts of December and that come January they will all be safely tucked away for another year.

Thank you Santa, and please don't worry if you feel unwell after all your exertions. There will be plenty of biomedical scientists at work, regardless of the date or time, to ensure that everyone who needs their services will be cared for.

Happy 2019 everybody.



Sarah May
Deputy Chief Executive

Institute of Biomedical Science is the professional body for the biomedical science profession.

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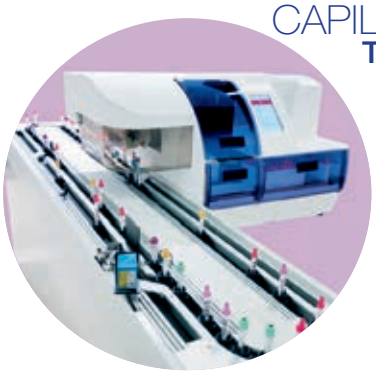

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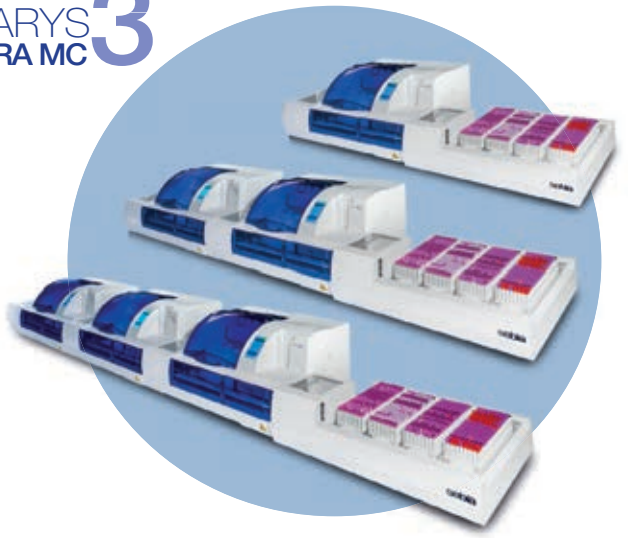

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SCIENCE NEWS

IN NUMBERS

10% increase in assaults

Physical assaults on NHS staff increased by nearly 10% last year. FOI requests were submitted to all 244 trusts in England, with responses received from 181. The trusts who responded reported a total of **56,435 physical assaults on staff** on 2016-17 – a **9.7% increase** on the **51,447** reported the previous year.

21%

The figures reveal that the biggest increase was in the acute sector, where **assaults were up by 21%**.

48.2%

Families sharing leftover antibiotics

In a survey of just under 500 US parents, **48.2% said that they kept, rather than disposed of, leftover antibiotics**. Of those, 73% subsequently gave them to siblings, unrelated children, and unrelated adults. Overall, **16% of participants** stated that they had **given their child adult medications**.

2 in 10

Microwavable instant soups and noodles cause at least two out of every 10 scald burns that send US children A&E departments.

The statistic is from new a paper presented at the American Academy of Pediatrics conference last month. Researchers determined scald burns related to instant soups and noodles affect **more than 9,500 children annually** in the US between the ages of four and 12 years. The peak age for these injuries was seven years old.

47%

of A&E attendances for sport-related injuries are made by under-19s.

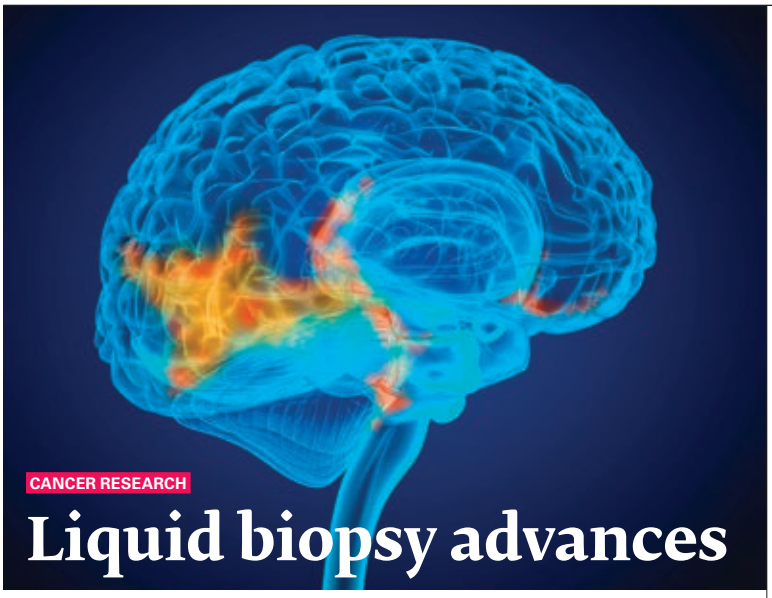
The figure is based on the analysis of data at two hospitals between 2012 and 2014. Researchers looked at **11,676 A&E attendances** for sport-related injuries at two hospitals in Oxfordshire. They found 10- to 14-year-olds were the group of children most likely to be injured, followed by 15- to 19-year-olds.

1,000

There are 1,000 epilepsy-related deaths each year in the UK.

About half of these are classed as sudden unexpected death in epilepsy (Sudep). This is when a person with epilepsy dies suddenly and prematurely with no reason for death. Sudep Action says **42% of deaths could be avoided** with improved annual risk check-ups.

SCIENCE NEWS



CANCER RESEARCH

Liquid biopsy advances

Scientists are making strides in developing liquid biopsies for brain tumours by detecting tumour DNA in the fluid from around the brain and spine.

The Cancer Research UK team analysed cerebrospinal fluid (CSF) in 13 patients with glioma brain tumours.

They detected tumour DNA in five (39%) of the patients.

The researchers used a cheap and widely available technique called shallow whole-genome sequencing to detect brain tumour DNA. They looked for large genetic changes, such as genes being duplicated or lost.

For the first time, the researchers identified tumour DNA in the CSF by looking at the size of the DNA fragments, which are shorter than those from healthy cells. This provides another way to detect brain tumour DNA, potentially increasing the detection rate.

In one patient, brain tumour tissue samples were compared to their CSF. The genetic changes broadly matched, but the CSF contained changes that were missed in some of the tissue samples, suggesting that CSF samples could reflect the repertoire of genetic alterations found in brain tumours.

→ **bit.ly/BS_DecNews01**

PROMOTING SCIENCE

NOMINATE SCIENTISTS FOR NEW £50 NOTE

The new £50 note will feature a prominent British scientist, the Bank of England has announced.

In addition to the Queen, the note will include the portrait of an eminent late scientist and the public are being asked for nominations.

There are currently 330 million £50 notes in circulation, with a combined value of £16.5bn.

The Bank's Governor, Mark Carney, said: "There is a wealth of individuals whose work has shaped how we think about the world and who continue to inspire people today. Our banknotes are an opportunity to celebrate the diversity of UK society and highlight the contributions of its greatest citizens."

A shortlist will be drawn up by a committee, including four science experts, and a final decision will be made by Mr Carney. Nominations can be made on the Bank of England website.

→ **bit.ly/BS_DecNews02**

STEM CELLS

SCIENTISTS CREATE BIODEGRADABLE SCAFFOLD

Scientists have created a tiny, biodegradable scaffold to transplant stem cells and deliver drugs.

It is hoped that the development may help treat Alzheimer's and Parkinson's diseases, ageing brain degeneration and spinal cord and traumatic brain injuries.

Stem cell transplantation, which shows promise as a treatment for central nervous system diseases, has been hampered by low cell survival rates, incomplete differentiation of cells and limited growth of neural connections.

Scientists from Rutgers University designed bio-scaffolds that mimic natural tissue and had good results in test tubes and mice, according to a study.

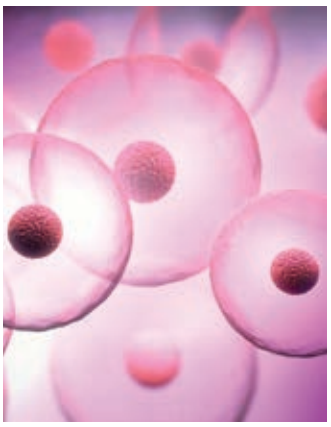
These nano-size scaffolds hold promise for advanced stem cell transplantation and neural tissue engineering. Stem cell therapy leads to stem cells becoming neurons and can restore neural circuits.

Senior author KiBum Lee said: "It's been a major challenge to develop a reliable therapeutic method for treating central nervous system diseases and injuries.

"Our enhanced stem cell transplantation approach is an innovative potential solution."

The researchers, who have been working with neuroscientists and clinicians, plan to test the nano-scaffolds in larger animals and eventually move to clinical trials for treating spinal cord injury.

→ **go.nature.com/2zC06ps**



IMAGES: ISTOCK/SHUTTERSTOCK

DNA ANALYSIS

SUPERMARKET SALAD AND ANTIBIOTIC RESISTANCE

Researchers from Germany have found that supermarket produce is a reservoir for transferable antibiotic resistance genes that often escape traditional molecular detection methods.

These antibiotic resistance genes might escape cultivation-independent detection, but could still be transferred to human pathogens or commensals.

The research, by a team from the Julius Kühn Institut, highlights the importance of the rare microbiome of produce as a source of antibiotic resistance genes.

Produce is increasingly recognised as a source of pathogenic bacteria, antibiotic-resistant bacteria, and resistance genes.

This study aimed to explore methods to characterise the transferable resistome – the collection of antibiotic resistance genes present in bacteria – associated with produce.

Salad, rocket, and coriander from German supermarkets were analysed by cultivation and DNA-based methods.

These results confirmed that cultivation-independent DNA-based methods are not always sufficiently sensitive to detect the transferable resistome in the rare microbiome.

→ **bit.ly/BS_DecNews03**

ARTIFICIAL INTELLIGENCE

HEALTH RESEARCH CENTRE

Scotland is to get a £15.8m artificial intelligence (AI) health research centre, called the Industrial Centre for Artificial Intelligence Research in Digital Diagnostics (iCAIRD).

The UK government has announced £10m of funding, with a further £5m due to come from partner companies.

The centre, which will be based in Glasgow, will focus on how AI could improve patient diagnosis and treatment.

It will bring together experts to explore AI in the treatment of strokes and some cancers.

It is hoped that using technology to process large amounts of data will allow the health service to operate more quickly and efficiently.

It is predicted that iCAIRD, which will have other bases around the UK, will create new jobs centred around AI and digital technology in healthcare.

WHAT'S HOT AND WHAT'S NOT

HOT

LLAMAS

Llama blood has been used by US scientists to produce a new antibody therapy that has the potential to work against all types of flu.

HOT

BRAZIL NUTS

Eating Brazil nuts may prevent weight gain and provide other cardiovascular benefits, according to two preliminary studies.

HOT

THE ANTARCTIC

Pioneering research carried out in the Antarctic into eye function and health under constant light or darkness has been published.

NOT

FIREWORKS

Fireworks packaging should show graphic injuries, say plastic surgeons, after firework-related A&E visits have doubled since 2010.

NOT

CPR

Researchers are investigating why bystanders are less likely to perform CPR on women than on men who collapse with cardiac arrest.

NOT

HOOKAHS

Smoking tobacco in a hookah, often seen as a healthy alternative to cigarettes, acutely impairs blood vessels' ability to function, shows research.

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RISK FACTORS

New markers for type 2 diabetes

The presence of death receptors in the blood can be used to measure the risk of developing cardiovascular diseases and type 2 diabetes.

The claim comes in a new paper published by a team from Lund University in Sweden.

The researchers found that people with known risk factors, such as high blood sugar and high blood fats, also have heightened death receptor levels.

Death receptors are activated, for example, in the case of infections when white blood cells that have combated a virus are to be removed.

It was previously known that death receptors in the blood can be measured, but not whether an elevated level was linked to increased cell death in type 2 diabetes and arteriosclerosis.

The results show that increased cell death can be linked to increased levels in the blood of three different members of the same "death receptor family" (TNFR-1, TRAILR-2 and Fas).

Increased cell death is seen in type 2 diabetes as well as arteriosclerosis.

High blood sugar and blood fats subject the body's blood vessels and insulin-producing beta cells to stress.

Long-term stress damages the cells and can cause the death receptors on the surface of the cell to trigger a cell suicide program within the cell.

→ **bit.ly/BS_DecNews04**

METFORMIN

MODE OF ACTION FOR DIABETES DRUG

Researchers have discovered a mechanism that may explain how the frontline type 2 diabetes drug metformin works to help cells better take up and use glucose.

The findings could potentially help explain metformin's action in preventing a variety of chronic diseases, including cancers.

Scientists at the Francis Crick Institute and University of Montreal developed a new method that analyses how all of a cell's biochemical processes respond to a particular drug at the same time.

The technology measures changes in the binding properties of all proteins to each other simultaneously. This enables scientists to identify molecular signatures that reveal how drugs influence cells.

This was applied to two metabolic drugs, one with a known mechanism of action, the immunosuppressant, rapamycin, and one with no known mechanism of action, metformin.

They found that metformin makes yeast cells act as if they are starved of the essential mineral iron. Further analysis revealed that metformin has a global effect on iron distributions in cells, which has a knock-on impact on iron-dependent biochemical processes.

→ **bit.ly/BS_DecNews05**

UNDER THE MICROSCOPE

This month: Publication bias

What is publication bias?
A type of bias that occurs when the outcome of an experiment or research study influences the decision of whether to publish or otherwise distribute it.

Has it been in the news?
It made headlines after the House of Commons Science and Technology Committee stated that, despite repeated warnings, not enough is being done to make sure the results of all clinical trials are reported.

How many clinical trials are going unreported?
A recent *BMJ* paper indicates that only 49% of recent research trails that should have reported their results have done so.

What is meant to happen?
Under EU rules, all trials on the European Union Clinical Trials Register should post results within 12 months of completion, but this has not been the case.

What's wrong with not reporting results?
The results of clinical trials are used to make real-world decisions about which treatments work best. Informed choices can't be made if the results of clinical trials are withheld from doctors, researchers, and patients.

What is the worst-case scenario of withholding results?
The government committee reported that in some cases it could endanger human life and cited the example of the anti-arrhythmic drug lorcainide, which was tested in 1980.

What's the story there?
Clinical trial results showed that people who were taking the drug were more likely to die than those who were not. However, the findings were not published until 1993 – long the drug was made available to patients in the US.

What will happen now?
MPs have called for The NHS Health Research Authority to produce a strategy for fixing this problem.

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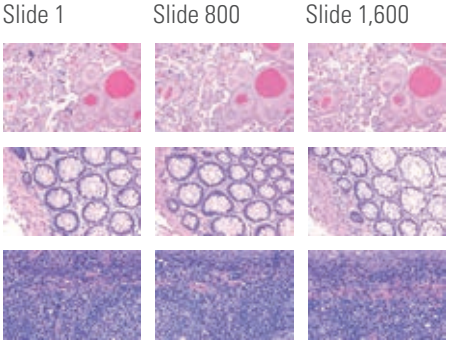

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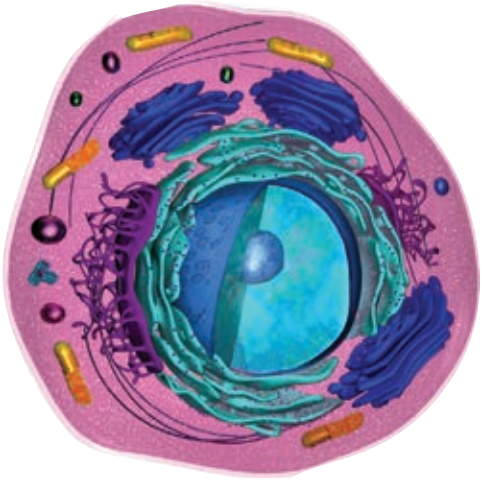

MEDISIEVE

MAGNETIC BLOOD FILTRATION

Medical device firm MediSieve was shortlisted for this year's Hammersmith and Fulham Brilliant Business Awards.

Nominated in the Best Tech Start-Up category, it was put forward by Upstream, a joint venture between Imperial College and Hammersmith and Fulham Council.

MediSieve was established in 2015, as an independent company, having spun off from University College London and its magnetic blood filtration system can specifically and selectively remove disease-causing agents from the blood.

The device targets the specific components that are behind the diseases, before taking them out of the patient's bloodstream.

→ **medisieve.com**

CLINISYS

STATE-OF-THE-ART PATHOLOGY

A new state-of-the-art laboratory system for the Black Country Pathology Service (BCPS) has been announced.

It is hoped the new laboratory information management system will reduce clinical risk and provide more complete patient history across primary and secondary care.

The new system will enable pathology services across the multiple hospital sites to work together more collaboratively than before.

CliniSys is delighted to have been selected by BCPS as their chosen IT solutions partner, having progressed through a rigorous and diligent procurement process.

→ **clinisysgroup.com**

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MEDICINES DISCOVERY CATAPULT

3D HUMAN CELL MODELS

Medicines Discovery Catapult and the Medical Research Council Centre for Drug Safety Science at the University of Liverpool are collaborating.

They have agreed a memorandum of understanding to combine their academic and industry expertise in developing next generation 3D human cell models and creating robust cellular platforms.

Through the collaboration these will be available to UK drug discovery SMEs.

The first project to be undertaken under the new alliance will focus on the development of a next generation cardiac safety model. The human cell model will enable companies to measure a broader range of patient relevant toxicities in a single assay.

→ **md.catapult.org.uk**

THE BIG QUESTION

THIS MONTH WE ASK

"What do you think 2019 will bring for pathology?"

Alison Geddis

President
Institute of Biomedical Science

Pathology has been the health service football for too many years and we're all in need of some respite from the relentless reconfiguration pressures and some recognition of the immense value our services bring to healthcare.

We're currently responding to a consultation on the proposals for how Essential Services Laboratories in England will deliver services and we will take every opportunity to use our experience to try and help shape this process.

This follows on from similar work in Northern Ireland and Scotland. We will continue to represent our profession at every level and ensure that our standards quality, safety, education and training are not disregarded in the quest for greater efficiencies and savings.

I believe we are entering the age of the consultant biomedical scientist. This has been an aspiration for a number of years, but it is finally becoming a reality. We will continue to work with the RCPath on the conjoint examinations, but I think that opportunities for biomedical scientist are set to expand considerably. If our health services are to maintain the expected high standards of care, new and emerging roles will be crucial and we are one of the most highly qualified and adaptable workforces within the NHS.

On a personal note, 2019 is Congress year and it will be our biggest and most ambitious programme ever. This is our opportunity to showcase the very best of what we do and I hope you'll be there to share the amazing experience with me.

IMAGE: IKON

Alison Cropper

Chair
British Association for Cytopathology

For those of us working in cytology, 2019 will bring the biggest changes there have been in the 36 years that I have been working in pathology.

NHS England are putting out to tender the whole cervical cytology screening programme in England for provision of a high risk HPV screening service, using cervical cytology as the triage test of HPV positive samples, which is expected to be around 15% of all samples. This huge reduction in slides will require far less screening personnel and services will be consolidated – a maximum of 13 contracts will be awarded in April 2019 following a competitive tender process.

NHS Improvement has been advising NHS England about the reconfiguration of cervical cytology services to try and align them with their recommended 29 Pathology networks, but quite how this will pan out is yet to be seen.

It is a most unsettling time for all staff working in cervical cytology, but according to NHS Improvement there should be no need for redundancies as staff can be redeployed within the emerging pathology networks, which are going to have workforce shortages. I hope this is the outcome and that the highly skilled cytology workforce we have is retained, if not in one of the HPV/cytology hubs, then within wider pathology services across the new networks.

For those who are awarded the HPV contracts, it will be a huge challenge to upscale to the new activity levels and put in place all the inter-trust linkages that are going to be required.

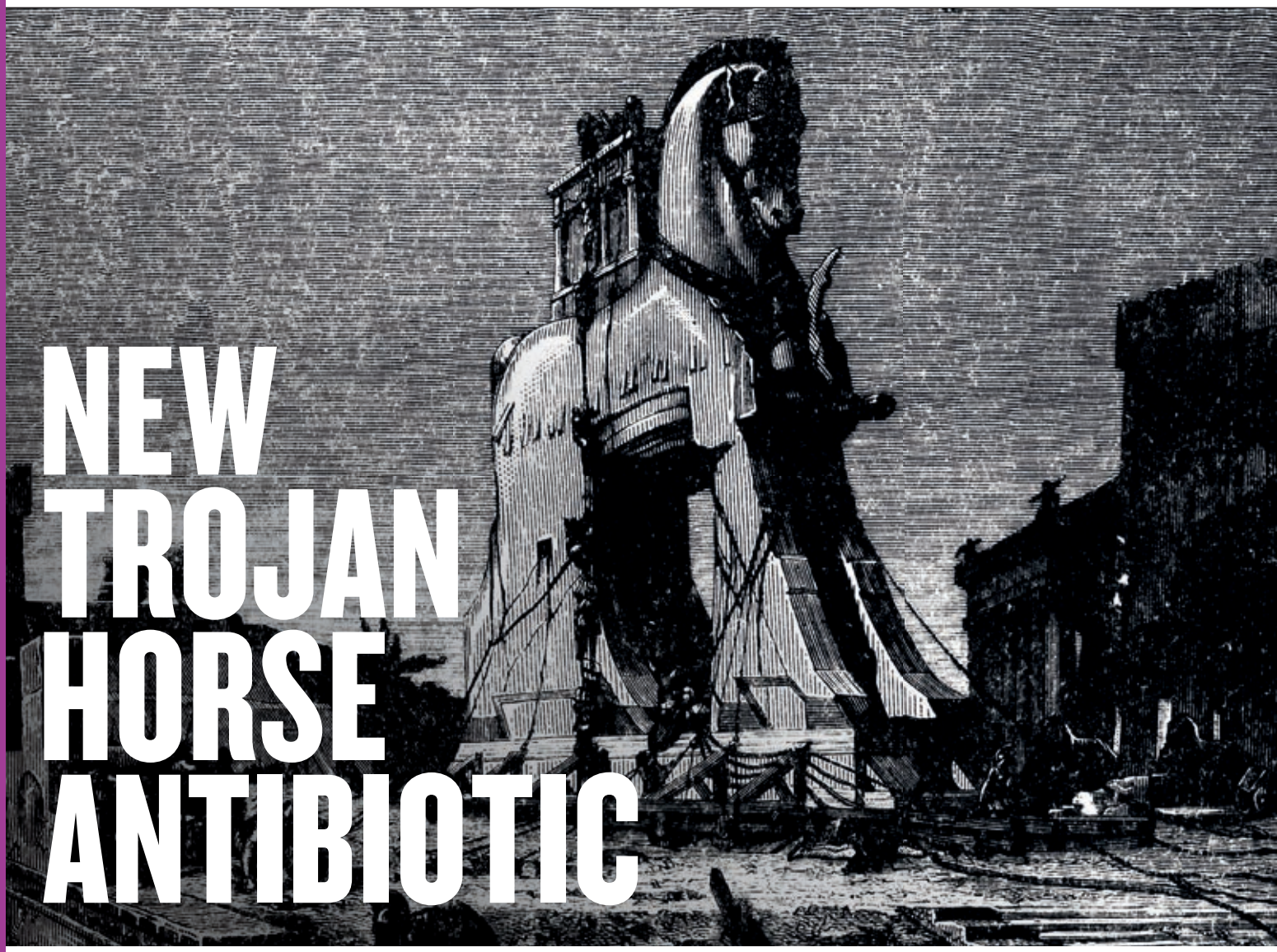
Ian S Young

Chief Scientific Advisor
Department of Health, Northern Ireland

It is an exciting time for pathology in the UK, with significant structural changes in the delivery of services and rapid technological advances. Now 2019 is almost upon us, and these two issues are likely to dominate the agenda.

In England, configuration of pathology networks and the roll out of genomic medicine centres will bring significant management challenges, but also opportunities to focus on reducing variation in access to pathology services and diagnostic tests across the country. Parallel processes are underway in the devolved nations, including Northern Ireland. Genomic medicine centres will build on the success of the 100,000 Genomes project, in which all four countries of the UK participated to offer an expanded range of diagnostic tests, including whole genome sequencing where it offers diagnostic advantages in rare disease diagnosis. Genetic testing will play an important role in the move towards personalised medicine, but the importance of other pathology tests in defining phenotype will also be recognised.

There will be increasing demand for pathology services delivered in the right place at the right time to optimise patient pathways, with input from the Getting It Right First Time leads in England. Digital pathology will be increasingly in the limelight, with discussion of how it can be coupled with artificial intelligence to transform tissue pathology. In this rapidly changing environment there will be more opportunities for Healthcare Scientists to take on advanced roles.



NEW TROJAN HORSE ANTIBIOTIC

Simon Portsmouth explains the latest trials of a hopeful new antibiotic and looks at the ongoing fight against drug-resistant bacteria.

Warnings about the ever-increasing threat of antimicrobial resistance (AMR) have been coming thick and fast in recent years. Most recently, in November, a report from the Organisation for Economic Co-operation and Development (OECD) called *Stemming the Superbug Tide* warned that over the next 30 years antibiotic-resistant infections could kill around 2.4m people around the world, including 90,000 here in the UK, adding almost £3bn to the cost of healthcare.

The OECD's simple remedy for the looming crisis is to promote better hand hygiene, curb the over-prescription of antibiotics, and test patients quickly to see whether they have bacterial or viral infections. It also claims that any investment in a package of such measures would pay for itself within just a year.

New antibiotic

Of course, another weapon in the arsenal is to develop newer and more robust antibiotics. But this approach doesn't come quite so quickly or cheaply – it can take up to a decade, with the costs running into millions, even billions.

While the funding and licensing environment for antibiotics may not be quite so attractive to pharmaceutical companies, that hasn't deterred the US arm of the Japanese firm Shionogi from "pursuing the development of novel treatments to combat this evolving threat".

It has been developing a new antibiotic called cefiderocol and its initial results were published in *The Lancet Infectious Diseases* journal in October.

Leading the Shionogi effort is its senior medical director, Dr Simon Portsmouth, who is not one to shrink from the danger posed by the spread of AMR. "This is clearly a real threat and already patients are dying with untreatable infections," he says, pointing to another report published in *The Lancet Infectious Diseases* in November. The piece from the European Centre for Disease Prevention and Control

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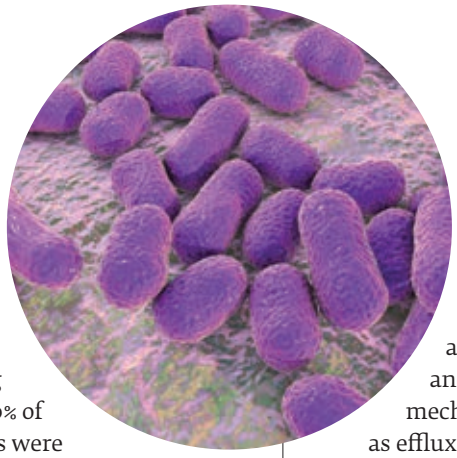


estimates the number AMR cases across Europe in 2015 and the resulting deaths. "About 70% of the 33,000 deaths were attributable to Gram-negative infections," says Portsmouth. "In Europe the deaths for AMR exceeded those for TB, HIV and influenza combined." The OECD report estimates that antibiotic-resistant infections are killing more than 2,000 people in the UK every year and almost 30,000 in the US.

Breaking down defences

The evidence for the rising menace of AMR is irrefutable, but instead of further alarming reports what's needed now is action from governments, healthcare agencies and the pharmaceutical industry around the world.

Shionogi's response began several years ago, with the development of cefiderocol in Japan, and Portsmouth's job has since been to perfect the new drug's efficacy and push it closer to commercial reality. "It was designed for Gram-negative AMR and designed to overcome β-lactamase activation and entry to the cell," he says. "Cefiderocol was designed to have stability against all known carbapenemases and was a response to AMR. It is a siderophore, with the iron chelating molecule that leads to active transport into the cell. Previous siderophores haven't reached human trials due to the rapid emergence of adaptive resistance, which isn't the case with cefiderocol."

The new antibiotic fights infections by infiltrating and breaking down the defences of the bacteria – a process that Portsmouth likens to a Trojan horse. "In infection, the immune system removes iron to starve bacteria of this essential metal," he says. "Bacteria produce siderophores naturally to scavenge free iron. Cefiderocol with a siderophore side chain highjacks or mimics this system to get transported into cells across the outer membrane and so overcomes some mechanisms of resistance, such as efflux pumps and porin channels – which are bacteria's natural defence either pumping drugs out or preventing their transport across the cell membrane. Once inside the cell, the structure of cefiderocol is stable to carbapenemases and works like any other cephalosporin antibiotic by binding to and inhibiting penicillin-binding proteins."

The trial

For the trial covered in *The Lancet*, cefiderocol was pitted against urinary tract infections (UTIs), which are the most common source of multiple drug-resistant Gram-negative infection. "The patients with complicated UTIs are a good population to study with monotherapy in a double-blinded manner," says Portsmouth. "This has been the common regulatory pathway for recent antibiotics undergoing streamlined development."

The results were encouraging. Portsmouth and his team hoped cefiderocol would at least match the performance of the well-established antibiotic imipenem and its sidekick cilastatin among a group of 452 patients randomly assigned either drug, but it actually scored a 73% success rate compared to imipenem's 55%. "We were pleased to see improved efficacy over a very good comparator antibiotic and able to demonstrate the favourable safety profile," says Portsmouth.

Some side-effects were noted, but they were more or less in line with the team's expectations. The most common was diarrhoea, though its frequency was no worse than with imipenem, they state.

The future

What's the next step in cefiderocol's promising development? "Further trials are ongoing in patients hospitalised with pneumonia and in carbapenem-resistant infections of the lung, urinary tract and blood stream," says Portsmouth. "We plan to submit a new drug application to the US Food and Drug Administration, followed by a marketing authorisation application to the European Medicines Agency and other countries." Anyone who wants to follow its progress can do so at clinicaltrials.gov under the identifiers NCT02714595 and NCT03032380.

The future looks positive for cefiderocol, so does that make somebody at the heart of the response to AMR feel optimistic? "The trial showed efficacy among a big group of patients, including some who had not responded to other antibiotics," says Portsmouth. "Further trials in more difficult-to-treat AMR are ongoing, but overcoming the threat of AMR will require more than just new antibiotics. That said, it is reassuring that we're making progress with the development of these drugs." BMS

SIMON PORTSMOUTH

- ✔ **1992** – Graduated in medicine from the University of Sheffield
- ✔ **2003** – Became an HIV specialist at St Mary's Hospital London
- ✔ **2008** – Worked on HIV-associated Kaposis's sarcoma and got an MD
- ✔ **2008** – Became a Fellow of the Royal College of Physicians
- ✔ **Present** – Moved into drug development for HIV and hepatitis C
- ✔ **Present** – Now working for Shionogi on cefiderocol and a new influenza antiviral.

FROM PROFESSIONAL TO PATIENT

Three scientists tell their personal stories of being diagnosed with chronic illnesses and how the transition from professional to patient has affected their work and lives.

ILLUSTRATIONS: GREG MEESON/HITANDRUNMEDIA.COM

STEPHEN MORTLOCK

Pathology Manager, Nuffield Health, Guildford Hospital

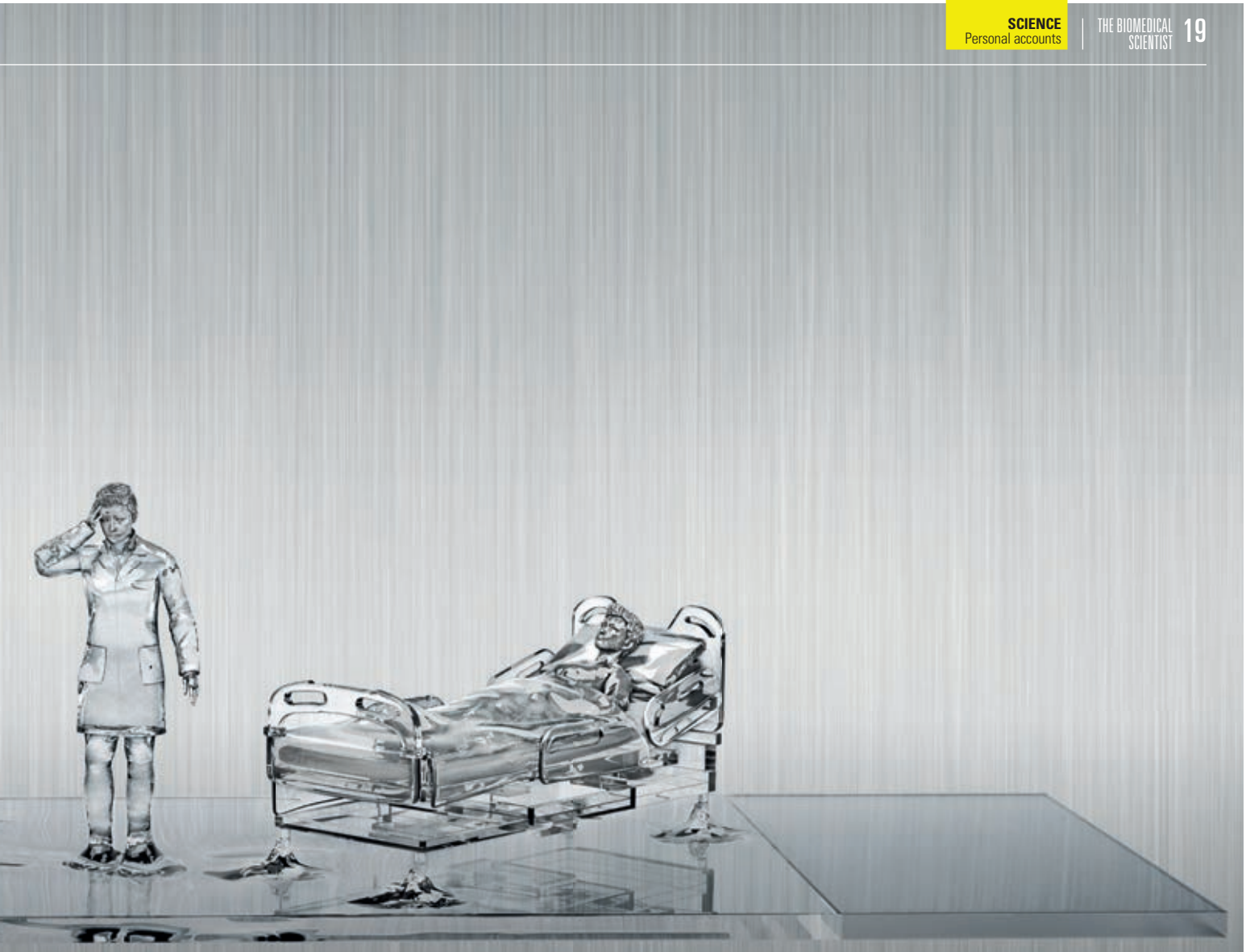
I like to think that as an individual that I am pretty fit. I don't drink or smoke, I exercise regularly and exceed my daily quota of fruit and vegetables. Then, in the middle of last year, I started to notice that I was more breathless than normal, with an annoying cough which didn't get better.

It all became slightly more alarming when I woke up one morning with a rapid erratic heartbeat, extreme breathlessness, my legs felt like lead and I had a general overall feeling of something not being right. I decided a trip to the emergency department was in order. After being poked, prodded and bled, I was sent off for a chest X-ray and transferred to the observation ward to wait for my results.

Later that day, the consultant came to tell me that my troponin levels and most of my other blood results were normal, but they had found an opalescence shadow down the right side of my heart, which would require further investigation. So the journey began.

Diagnosis

I went back to the hospital the next day for a contrast CT scan using iodine dye. A couple of hours after the scan was completed, I was called into the consultant's office where he was waiting



with a Macmillan nurse, which seemed to herald bad news. Surprisingly, the revelation did not affect me as I thought it would have done. They had found a tumour in my right lung, not my heart. It was quite large (about 8-9 cm at the widest point) but it was a single tumour. Driving home from the hospital seemed to take forever and I had to break the news to my wife Caroline and the rest of my family and, of course, the team at work.

Now everything moved up a gear and the next few weeks were a flurry of further blood tests, investigations, different examination tables and sitting in waiting rooms reading week-old magazines. There was a lung function test, a PET scan and an MRI of my head to narrow down the options of the type of tumour that was growing in my chest. Appointments were made to see different consultants, as each new investigation revealed something new. Finally, the last investigation was a CT-guided biopsy of the affected lung at the day surgery unit.

Eventually, we had a diagnosis. It was a stage 1E diffuse B-cell lymphoma (non-Hodgkin's lymphoma) in my right lung, with an associated build-up of pleural fluid. From initial diagnosis to the identification and then to my first cycle of chemotherapy was only five weeks. At every step, and for every investigation, I was included in the discussions and when discussing the available options. I must have asked thousands of questions.

Treatment and effects

With a diagnosis made, the consultants could decide on the suitable therapy. Luckily, there was not to be any surgery, but six cycles of R-CHOP chemotherapy on a three-week cycle. R-CHOP is a combination therapy of rituximab, doxorubicin, vincristine, cyclophosphamide and prednisolone. But the rituximab took four to five hours to infuse and the whole treatment effectively lasted all day. Then the treatment cycle was over until the next time. There were also the take-home medications, two days of ondansetron, four days of prednisolone and three weeks' worth of acyclovir and co-trimoxazole.

The first 48 hours after treatment seemed to be OK, but usually by the morning of the third day I was feeling lethargic, slightly nauseous and all my muscles ached. Then it got worse.

People have told me that you should be able to go to work in the periods between treatments, but there was no way that I would have been able to do anything constructive at work. However, on my better days

I was able to work from home and keep up to date with emails.

Neutropenia

One of the problems I encountered was that after cycle two of the chemotherapy, my white blood cell count did not return to normal, so I had periods of neutropenia. As a result, over the course of the treatment, I had two separate chest infections treated with oral antibiotics and then I developed septicaemia, which was treated with IV tazobactam. To counter the neutropenia, I was prescribed filgrastim that they hoped would regulate the production of neutrophils within the bone marrow. This was a self-administered injection for me to take home after each chemotherapy cycle, five days of injections each time.

Side effects

I lost what little remaining hair I had on my head, most of my body hair went and also my eyebrows, eyelashes and nasal hair. Then there was the tiredness, lethargy, muscle aches and cramps, nausea and, of course, the alternating bouts of constipation or diarrhoea, flatulence and haemorrhoids.

Then there was the evening I was injecting the filgrastim and that leg went into severe cramp. I had my tracksuit bottoms around my ankles, a hypodermic syringe sticking into my leg and was hopping around trying to relieve the cramp. It was both disturbing and comic.

Two days after my second cycle of chemotherapy, one of my teeth cracked, leaving me with a rough exposed hole. Since I couldn't visit my dentist we decided to get a temporary filling kit from the supermarket. I was lying on the sofa shining a torch in my mouth while my wife filled the tooth with putty.

On Christmas Day, rather than being with our families, we spent the day by ourselves with me alternating between shivering on the sofa and rushing to the toilet.

The end in sight

My journey is not over yet, but the end is in sight. The lymphoma has shrunk from its original size to a few small non-viable cells residing in the lower part of my right lung. I will be under the care of the hospital for the next few years with regular blood tests, scans and reviews.

But now, having been on the receiving end of hospital investigations, it has highlighted the old adage that behind every sample is a patient, in this case it was me. I'm not the first person to have diffuse B-cell lymphoma and, I'm afraid, I won't be the last, but this journey has altered my perspective. I am always ready to pass on my experiences; to encourage newly diagnosed patients and tell them that although the treatment can be bad there is always hope.

I still have lingering after effects of the chemotherapy and radiotherapy but my body should continue returning to normal over the coming months. On the plus side, I don't feel sick all the time, I don't fall asleep while I'm eating breakfast and if I go for a walk I don't fall over my feet and my body temperature doesn't fall below 35°C. Also, I am now able to walk for more than five minutes without needing to sit down for a rest.

It is difficult to know how to thank everyone who has been involved in my diagnosis and recovery but certainly my thanks go to everyone at Frimley Park Hospital, from phlebotomy to pathology, but especially the chemotherapy nurses whose good humour made treatment day bearable and to the Macmillan nurses who were there to offer advice. A big thank you goes to the matron and the staff at Guildford Nuffield Health who continue to support me through my absences from work and follow-up appointments. But most of all my love and thanks go to my wife Caroline, my family and friends who were always there during my darkest hours when the outlook seemed very bleak.

"I had needles and tubes galore stuck into me and was tested to oblivion and it made me appreciate what repeat testing means"

NICK KIRK

Principal Information Analyst, Royal Papworth Hospital NHS Foundation Trust

After spending 31 years working in pathology and dealing with other people's diseases, it comes as a bit of a shock when you find yourself at the other end of the equation.

I have been a type 2 diabetic for over 20 years, and 18 months ago this led to total kidney failure. Within a week I went from being "normal" to being at death's door. An emergency admission to Peterborough City Hospital found me on the cardiac ward

with cardiac failure, connected to a bank of machines that go "ping" and an oxygen supply with a series of doctors looking over me with very concerned faces.

They managed to pull me back from the brink on two occasions, which then led to a three-week stay on the renal ward, where they tried to "dry" me out. In those three weeks they removed over 40 litres of fluid from me through a combination of diuretics and dialysis.

I had needles and tubes galore stuck into me and was tested to oblivion and it made me appreciate what repeat testing means to a chronically ill patient, something I may not have fully appreciated in the past. It also made me appreciate more the implications of rejecting samples and requesting a new blood sample.

The constant testing became a real burden after a while and even though the phlebotomists were total professionals, the sight of one at my side room door made my heart sink.

The impact

Once I had recovered enough and had returned to "normal", I had an arterio-venous fistula constructed in my left wrist to allow easy access for haemodialysis. I now have dialysis three times a week after work, which has meant that my social life has taken a real knock. Fortunately I can flex my hours at work to accommodate the dialysis, which allows me to still work full time. It is tiring though.

My current condition now requires regular clinic attendance and Doppler scans of my AV fistula, all of which is time-consuming and has an impact on my job, as it has led to me having to use a number of annual leave days to cover these absences.

Mindset

Having kidney failure has turned my life upside down and my on-going treatment dominates my life. It restricts where I can go and for how long. Currently, the longest holiday I can take is two and a half days, which limits me to only going short distances away from the hospital. Fortunately for me, that includes the North Norfolk coast, one of my favourite places in the UK.

Most people think of themselves as indestructible and certainly coming from a pathology background, you perceive many of these diseases and conditions you deal with as things that happen to other people, not to you. When you find yourself in the position I have, you have to approach life with a totally different mind-set than before, which takes a lot of getting used to.

HEDLEY GLENCROSS

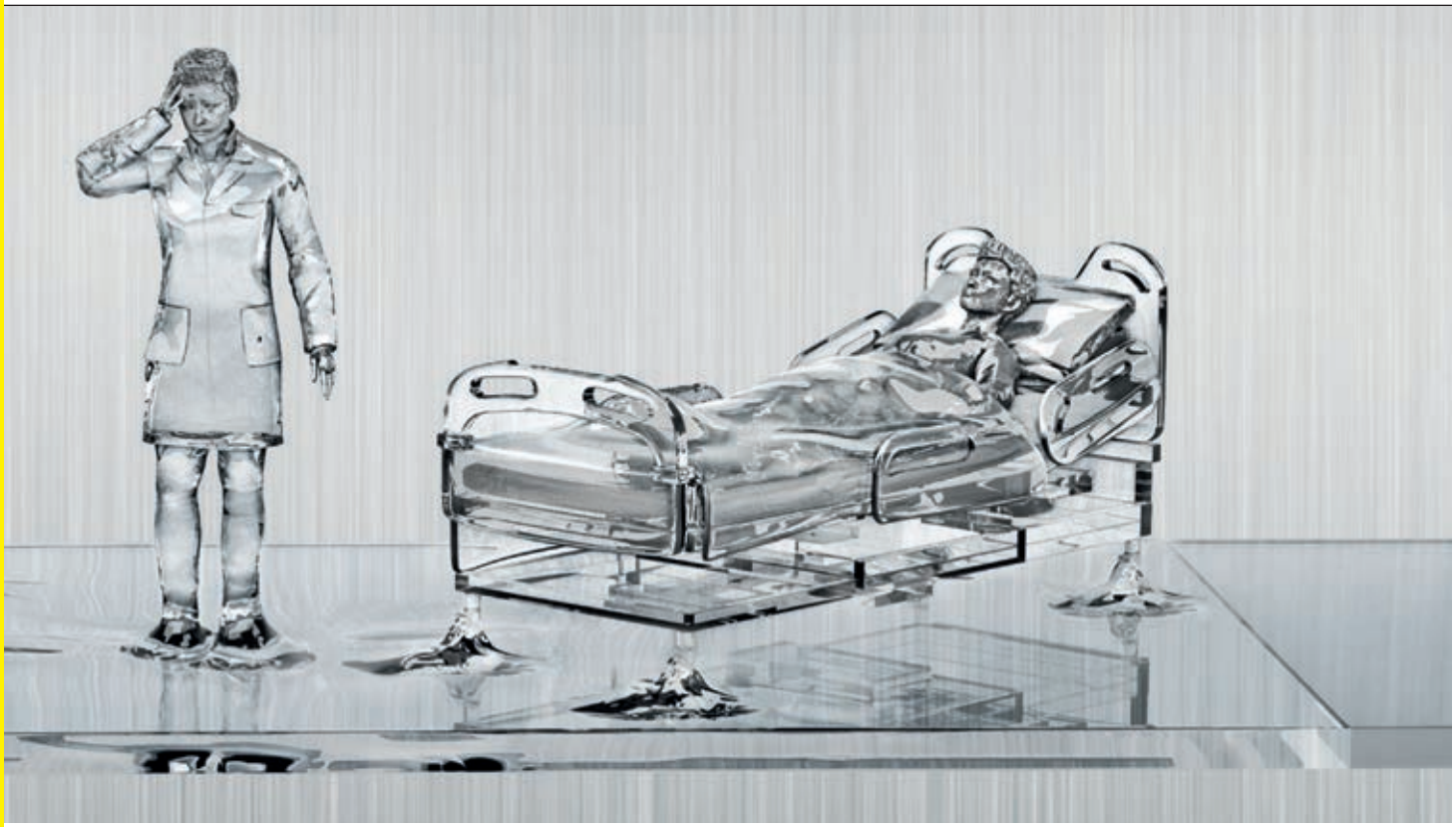
Advanced Specialist Biomedical Scientist, Portsmouth Hospitals NHS Trust

I was diagnosed with testicular cancer when I had recently turned 34, at the culmination of a number of stressful life events. I had recently moved house, having secured my first laboratory manager job, some 12 months previously after working away from home for over eight months.

It was very difficult as at the time of my diagnosis my son was just under two years old and among a large number of worries was the possibility that I would not see him grow up.

Aware of issues

I've never told any of my family this, but I was aware of something being wrong for a few months prior to my definitive diagnosis. Even before I got my new job, I would arrive at home, pick up my



son for a "hello" and nod off to sleep almost immediately, I also suffered from regular short-lived colds, but of course this was just stress-related, wasn't it?

Finally, I started to become uncomfortable and my right testis was feeling heavy, however; like men in general, I dismissed it thinking it would get better. But, being a good biomedical scientist and cytologist, I researched things and finally it was a single phrase in a cytology textbook that gave me the answer: "Painless hard lumps or alterations in size or weight of a testis are always suspicious". This summed me up to a tee and prepared me for the worst news. Looking further, I fitted a classic presentation history.

Coincidently, at that time, my son in his excitement jumped on me after a Sunday afternoon walk, creating some trauma in that area (ouch), which gave me an excuse to visit the doctor. Glad you did that Joe.

Motivation

The upshot was removal of my testis, a CT scan that showed lung metastases and an ensuing gruelling six-month course of chemotherapy with all its wonderful side-effects, sickness, hair loss and the like. Even when I was better, I had a blood test on my first day back at work, some two or three weeks after finishing chemotherapy and strongly against the wishes of my oncologist, and my Hb was 60g/L. Basically in its boots, but I felt wonderful.

Yes, you can get through major illness and come out the other side a more positive person. Being this ill was the spur to do other things and make something of my life, rather than just ambling along as perhaps I had done up to that point.

Achievements

I can trace back to this event the reasons why I became an IBMS Council member, serving 10 years (and a further eight years as an IBMS employee), seeing projects I was involved in or initiatives I helped start, that are still part of the profession. It is also why I was lucky enough to get to work in Sweden with one of the arms of the Swedish Two-Counties Breast Screening Programme. Why I have edited and co-authored a book, why I have published papers, why I have taught and lectured widely. It is also why I remain active professionally as an executive committee member of BAC and why I am involved with a UN-funded project to set up a cervical screening programme in Moldova.

Next year it will be 30 years since my diagnosis. Doesn't time fly by... IBMS

Yes, you can get through major illness and come out the other side a more positive person

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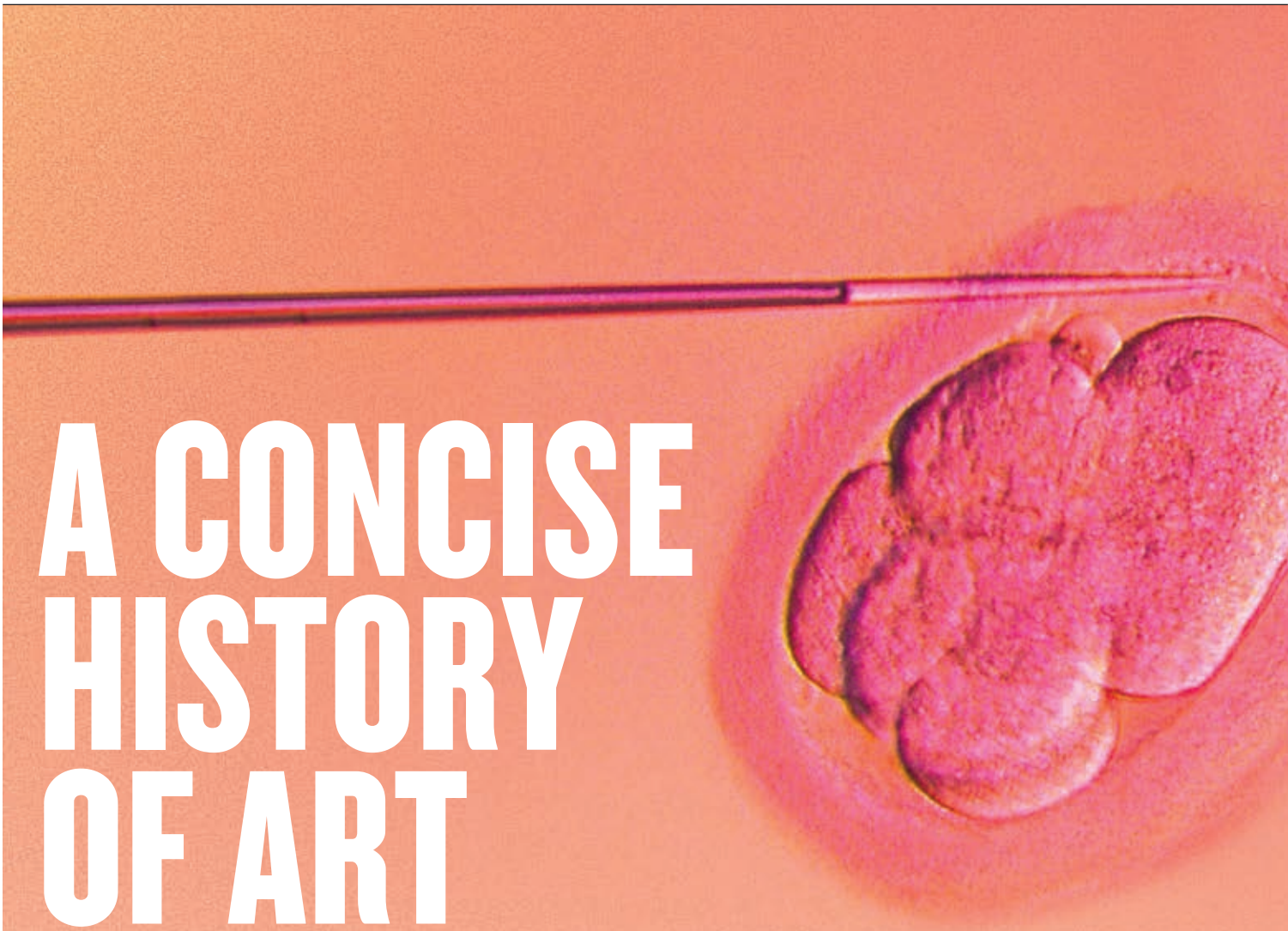


A CONCISE HISTORY OF ART

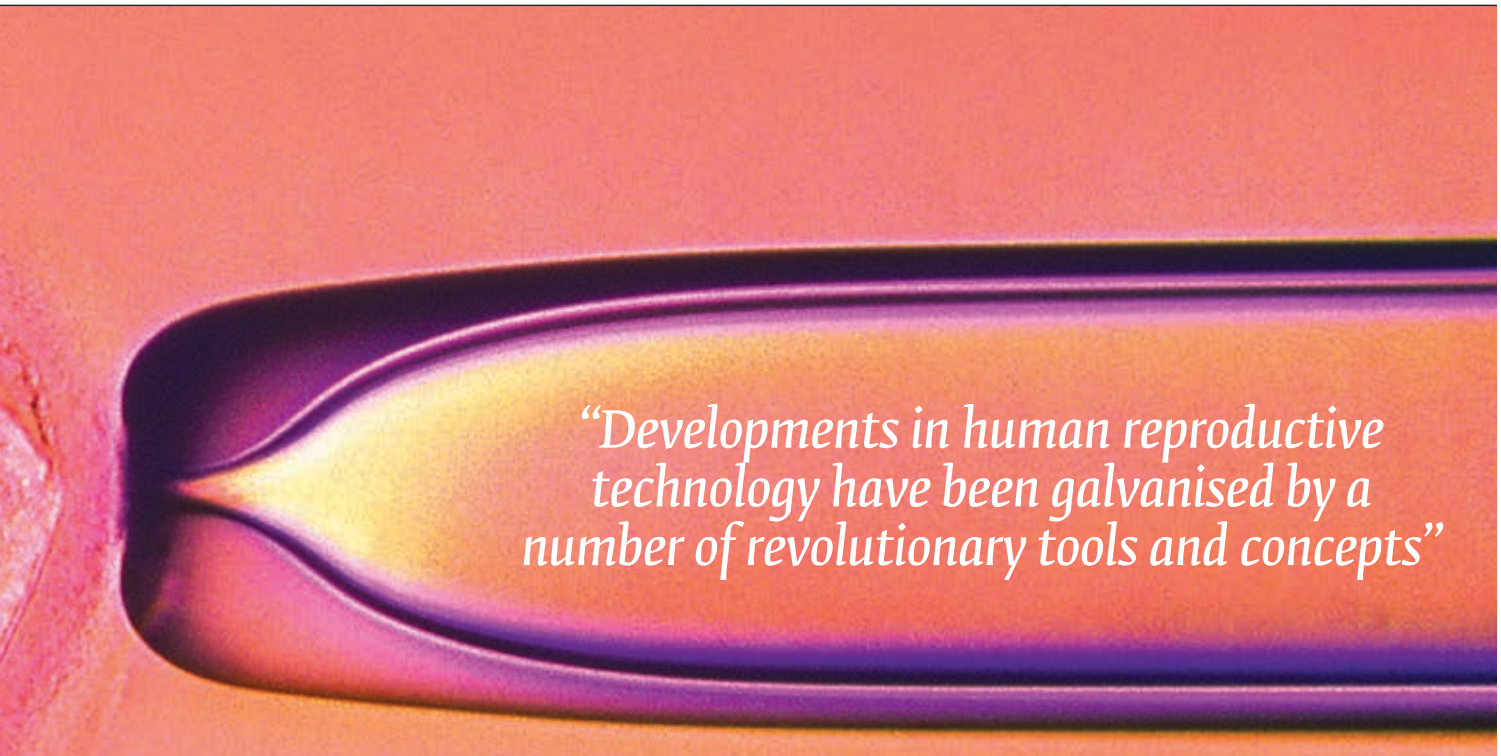
To mark the year that the first test tube baby, Louise Brown, turned 40, independent researcher **Zara Josephs**, looks back over the history of artificial reproductive technology.

Theories of conception have always abounded, from pre-historic ideas about fertility goddesses to the nature-based explanations of the early Greek philosophers. Such theories included pangenesis, in which the germinal cells were postulated to originate from the whole body; spermism, which held that the structure and form of offspring, were contributed solely by the male parent (the female providing only nourishment); and the particularly popular preformationism, in which a miniature human housed in the sperm developed in the female's womb following implantation, emerging in due course as the neonate.

Aristotle, the first to formulate a coherent theory of conception, saw the sperm as containing a pre-existing "principle" for specifying the generation of new offspring following a specific blueprint. The important point was that this principle (to be identified millennia later as the genetic code) for the building up of the organism was something other than the material constituting the final form of the organism.

In 1677, Antonie van Leuwenhoek (hailed as the father of microbiology) became the first person to observe and describe sperm cells. Karl Ernst von Baer discovered the mammalian ovum in 1827, while Edgar Allen was first to observe the human ovum in 1928. The first reported fertilisation event, recorded in 1876 by Oskar Hertwig, was the fusion of spermatozoa and ova in starfish.

Successful engineering of the fertilisation process was first observed with Lazzaro Spallenzani's artificial insemination of dogs in 1780, a feat that



"Developments in human reproductive technology have been galvanised by a number of revolutionary tools and concepts"

was followed a decade later by Dr John Hunter, who performed the first recorded artificial insemination in humans. In 1963, Chang and Yanogumachi demonstrated, through experiments in hamsters, that *in vitro* fertilisation (IVF) lay within the realms of possibility.

Human IVF was made possible by collaboration between Robert Edwards, Patrick Steptoe and Barry Bavister, which led to a 1969 *Nature* paper describing the *in vitro* fertilisation of human eggs.

The continuing collaboration of Edwards, Steptoe and Jean Purdy eventually led to the birth of Louise Brown on 25th July 1978.

Developments in human reproductive technology have been galvanised by a number of revolutionary tools and concepts, including the polymerase chain reaction (PCR); recombinant DNA techniques; transgenic technology; somatic cell nuclear transplantation; and microRNAs. These tools have enabled the further refinement of disease prevention and treatment strategies. Techniques dealing specifically with infertility all come under the heading of artificial reproductive technology (ART): the *in vitro* manipulation of sperm, eggs or embryos in order to achieve successful fertilisation, implantation and clinical pregnancy.

IMAGES: SCIENCE PHOTO LIBRARY/GETTY

Oocytes and ageing

Much of ART has focused on women, for reasons that appear obvious: while men continue to produce sperm cells throughout life, women are born with all the egg cells they are ever going to produce, and these decline with age, in both quality and quantity. Furthermore, older age at conception is a risk factor for chromosomal errors in the embryo, which can cause miscarriages or the birth of a child affected with a genetic disorder. The most common of these disorders is trisomy 21 (Down Syndrome), which is linked with mental and physical problems and a shortened lifespan.

Most chromosomal errors arise during meiosis, the cell division that produces haploid eggs or sperm cells from a diploid stem cell. Eggs are formed in the ovaries of the fetus before birth, and their number declines continually from birth until menopause. Pioneering work by Hartsherne and others has shed light on mechanisms underlying chromosomal aberrations in older mothers. Chromosome pairs are held together by binding molecules which are laid down prenatally. In meiosis 1, two chromosomes must arrive at the same spindle pole; in meiosis 2, they have to separate. Thus the binding proteins must be flexibly adhesive. With time, these binding molecules disintegrate, and in older eggs come unstuck. By the time the chromosomes segregate just before ovulation, they have been in an arrested state for many years. The kinetochores (protein clusters) which attach chromosomes to the spindle tubules control the orientation of the chromosome attachments and ensure that the chromosomes are pulled in the right directions at meiosis 1.

In older women, the paired kinetochores are further apart at metaphase of meiosis than in younger women. Thus, in humans, kinetochores move apart with time, a fact linked with the higher incidence of chromosomal aberrations in fetuses of older women. Significantly, in species such as mice, in which the kinetochores are fused together (and thus held firmly together during the pre-birth meiotic arrest), chromosomal anomalies occur far less frequently than in humans. Women planning to delay conception are currently advised to avoid risk by

banking their eggs while still young, for later use; or by accepting eggs from younger donors.

Male fertility testing

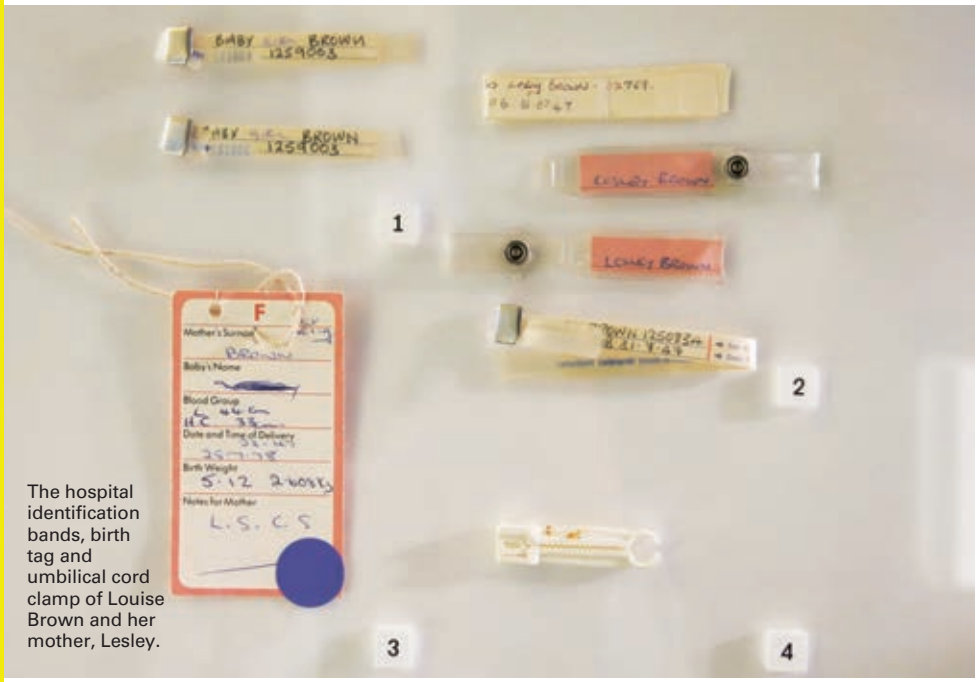
The relative lack of attention to male fertility notwithstanding, the evidence shows a link between increased paternal age and declining fertility, as well as serious birth defects. In fact, 50% of infertility cases arise from poor sperm function, yet diagnostic and management tools for male infertility are few in number.

The main diagnostic tool is semen analysis using reference figures published by the World Health Organization (WHO), which allows classification into different categories: normal (normozoospermia); reduced motility (asthenozoospermia); containing high numbers of dead sperm cells (necrozoospermia); displaying morphology abnormalities (teratozoospermia); low in count (oligozoospermia); and zero count (azoospermia). However, the WHO criteria leave many cases of male infertility unsolved. Thus, the new assay developed by Dimakopoulou and Jayasera at Hammersmith Hospital, London, is a welcome development. High levels of reactive oxygen species (ROS) are known to be a leading cause of male factor infertility. Based on the association of ROS with cell pathology, the new chemiluminescence-based test directly assays ROS through measuring light emitted following the oxidation of luminol. While the endogenously generated ROS in sperm cells promotes sperm motility and egg fertilisation, excessive ROS levels can peroxidise the sperm plasma membrane and damage DNA in both nucleus and mitochondria. The result is dysfunctional sperm that are incapable of fertilising eggs. The ROS assay is especially relevant for men leading harmful lifestyles or harbouring infections. The medical consensus is that management by antibiotics and by reducing dietary fat intake may be valuable for couples with unexplained recurrent miscarriage.

Steps to fertilisation

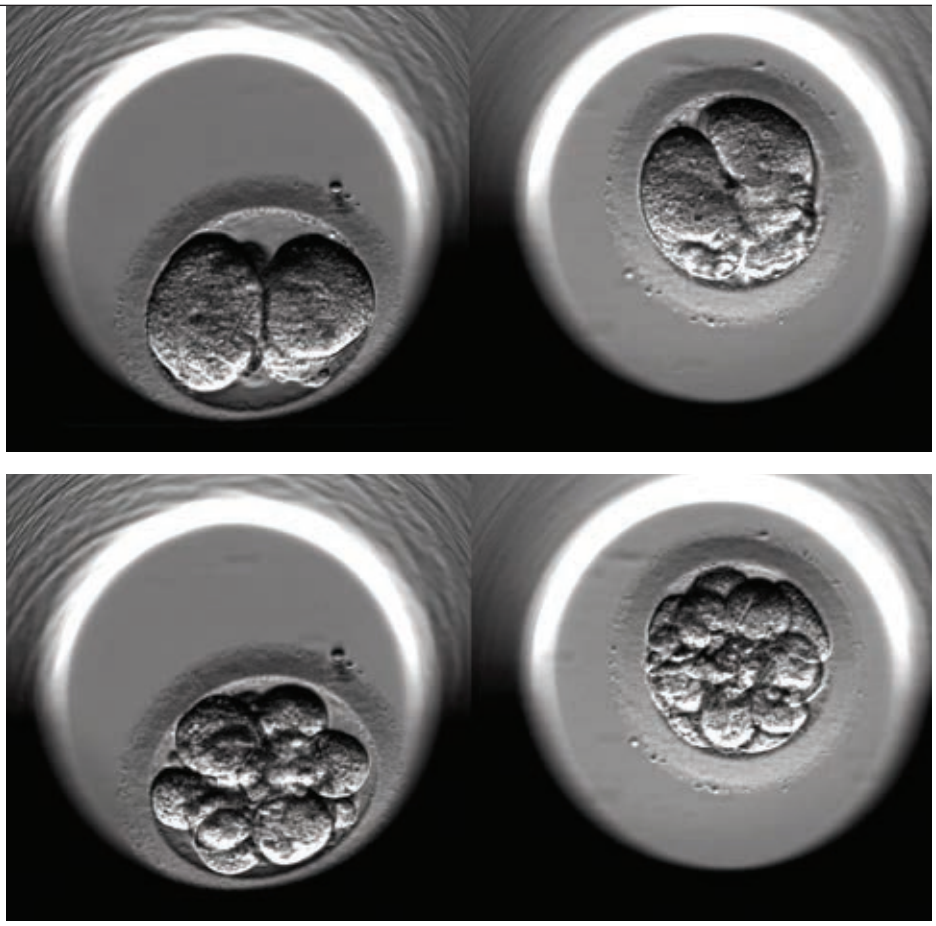
The expression "miracle of birth" is aptly worded: many steps can and do go wrong between gametogenesis and birth. Any break in the chain of events leading to fertilisation will derail the process. First, the sperm cells (approximately 180m in each ejaculate) navigate towards the egg cell through the hostile environment of the female reproductive tract, suffering immune system attacks en route. The few sperm cells that arrive at the utero-tubal junction unscathed undergo a multi-step selection and activation process to ensure error-free fertilisation:

- Capacitation: The first of these steps, takes place in the fallopian tube reservoir. Here, spermatozoa undergo molecular changes that trigger hyperactivity and greatly increased motility that propels them towards the ovum in the *ampulla*. Capacitation also involves destabilisation of the sperm's cell membrane in readiness for the next step.
- Acrosomal reaction: The egg is ringed by the *zona pellucida*, a protective glycoprotein coat which contains receptors for sperm cells. Contact of the sperm with the *zona pellucida* elicits the fusion of the sperm membrane with the acrosome, a cap-like organelle at the tip of the sperm cell. The fusion releases enzymes that break down the *zona pellucida*, allowing the sperm to bind to the egg cell membrane and initiate fertilisation.
- Cortical reaction: As soon as the first sperm cell fuses with the egg, the egg releases cortical granules that deactivate all sperm receptors, preventing penetration by any further sperm cells (fertilisation by more than one sperm - polyspermy - almost inevitably leading to early embryonic death).
- Meiosis reactivation: The oocyte, hitherto suspended in metaphase of meiosis 2, is released from meiotic arrest though signals carried in calcium oscillations triggered by the sperm-egg fusion.
- Nuclear fusion: The sperm and egg nuclei migrate towards each other along a pathway of microtubules derived from



The hospital identification bands, birth tag and umbilical cord clamp of Louise Brown and her mother, Lesley.

IMAGES: GETTY



Right. Cell-division of two fertilised human embryos during the third day of embryonic development following IVF treatment at a private clinic in London.

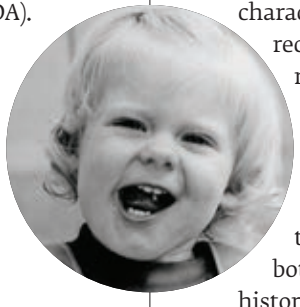
both sperm and egg, fusing to form the diploid zygote nucleus.

The sperm factor

The theory holds that sperm contain a specific trigger that initiates conversation between the two gametes when they meet. This "sperm factor" was identified as a unique phospholipase C (PLC) form called phospholipase zeta (PLCζ), found in the sperm's cytoplasm. PLCζ, activated by fertilisation, triggers calcium release from the egg's endoplasmic reticulum. Thus, it mediates communication between sperm and egg. The calcium is released in a characteristic oscillatory pattern. Research shows a link between infertility and PLCζ absence, deficiency or abnormal localisation. Thus, PLCζ assays enabling detection of egg activation ability have been developed, which clinicians can use to develop appropriate clinical management strategies.

AOA as male infertility treatment

New diagnostic tools to treat oocyte activation deficiency (OAD) have been developed to diagnose and manage cases of infertility that fall outside the WHO criteria. Many couples with a history of fertilisation failure have benefited from artificial oocyte activation (AOA). In this process, an artificial agent is applied to the oocyte during conventional intracytoplasmic sperm injection (ISCI), to induce calcium release and initiate activation events. This method may improve fertilisation outcomes in azoospermic males, or couples for whom conventional ISCI has failed. However, AOA fails to replicate the natural pattern of calcium oscillations (instead, releasing the Ca^{2+} all at once), or the control of gene expression in the embryo characteristic of PLCζ, and could therefore exert a negative impact on the developing embryo.



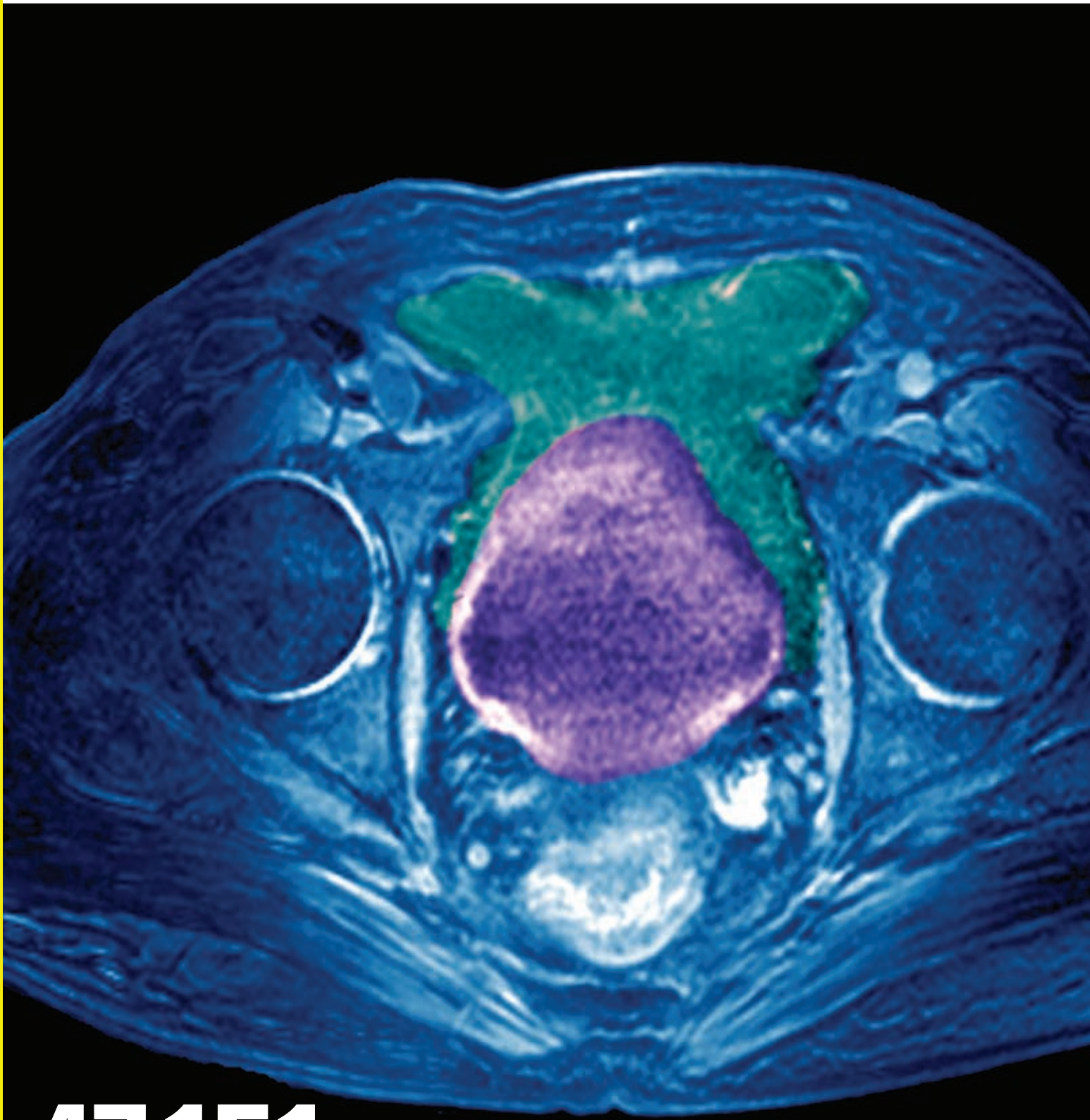
Research is ongoing into recombinant PLCζ, which may better mimic the effects of the naturally generated kind.

From A to zeta

Aristotle postulated a conception theory that in principle agrees with the discoveries today, almost two thousand years later. Over the intervening centuries, major breakthroughs in knowledge appear to have been characterised by the same recurrent principles: a wide-ranging curiosity, multidisciplinary training, fruitful collaborations and an element of serendipity. Aristotle made contributions to the fields of biology, botany, chemistry, ethics, history, metaphysics, philosophy, physics, politics, psychology, rhetoric and zoology. He also founded formal logic. Leuwenhoek and Spallanzani were also polymaths. Louise Brown's birth was made possible by collaboration among many scientists around the world. The story continues to unfold and in this digital age the possibilities it holds are endless. As an example, a recombinant PLCζ may be the solution to infertility for many aspiring parents. However, a single mature human sperm contains over 1,700 functional proteins, any of which it might be a potential therapy target, as might be any of the hundreds of egg proteins.

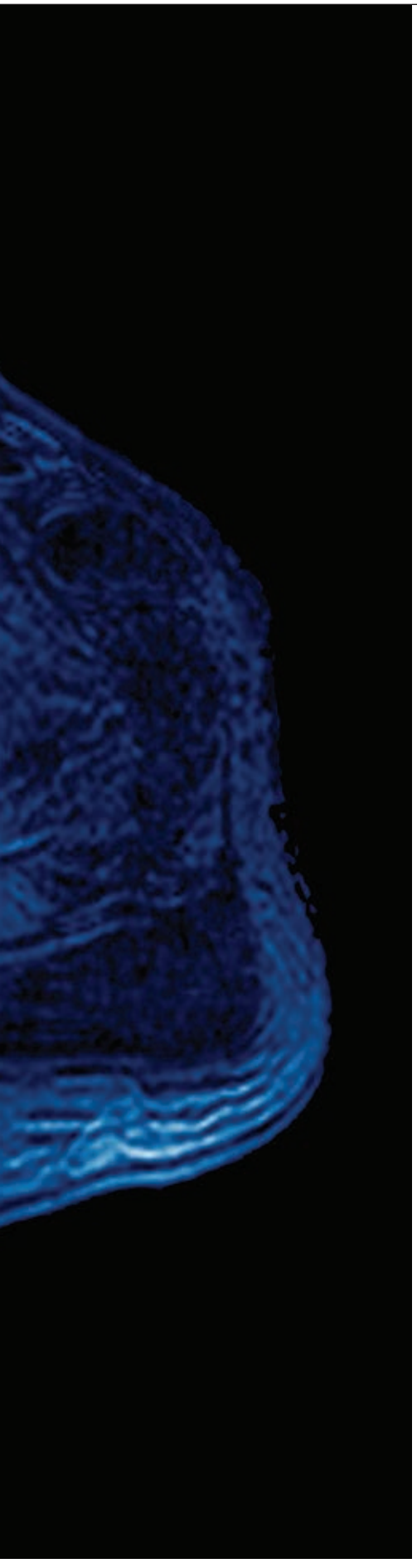
This paper has described management strategies for women who delay childbirth until later in life; health advice for men with infections or harmful lifestyles; new diagnostic tools for male infertility; and the potential for important breakthroughs due to the deployment of molecular biology tools. Polymathy, a trait linked with ground-breaking discoveries, is increasingly discouraged in the current era of specialisation. However, given the explosion of data growth and knowledge across different fields, interdisciplinary collaboration is essential for optimal progress in this, as in any other, field. BMS

Zara Josephs is an independent researcher, specialising in clinical biochemistry and molecular pathology.
To see the references, view the article online at **thebiomedicalscientist.net**



47,151

THERE WERE **47,151 NEW CASES** IN 2015 WITH **11,819 DEATHS** DUE TO PC. THERE IS AN INCREASED RISK OF PC WITH AGE AND OVER ONE THIRD OF CASES ARE IN THE 65-74 AGE GROUP



Left. Coloured magnetic resonance imaging scan of a section through the pelvis of a 65-year-old patient with prostate cancer.

IMAGE: SCIENCE PHOTO LIBRARY

CLINICAL CHEMISTRY CLASSICS

TUMOUR MARKERS

This series on tumour markers concludes with a review of pioneering work in the development, analysis and clinical application of an important serum tumour marker – prostate specific antigen.

Prostate cancer (PC) is the most common cancer in males and constitutes around 26% of all cancer related deaths in the UK. There were 47,151 new cases in 2015 with 11,819 deaths due to PC. There is an increased risk of PC with age and over one third of cases are in the 65-74 age group, with a higher incidence in black males. Clinical features may be absent or include some of the following symptoms: urinary retention, frequency, nocturia, haematuria, impotence and weight loss meriting further clinical and laboratory investigation. The clinical process for diagnosis generally includes basal serum prostate-specific antigen (PSA), digital rectal examination (DRE) with palpation for any surface irregularities, especially a nodule, transrectal ultrasonography (TRUS) which may reveal benign prostatic hyperplasia, or suspicious hypoechoic areas which require TRUS guided needle biopsy and histological interpretation for a Gleason score. With a strongly positive diagnosis, an early isotopic bone scan may be performed. Around 20% of patients with PC have metastases at diagnosis with bone, liver or lung secondaries most common, with a five-year survival rate of around 29%, this increases to almost 100% if the detected tumour is local without metastases.

An early prostate biomarker

In 1935, Kutscher and Wolberghs at Heidelberg University reported that prostatic tissue and seminal fluid contained a high concentration of a phosphatase with optimal activity between pH 4.5-6. Alexander and Ethel Gutman adapted the King Armstrong colorimetric method for alkaline phosphatase with an acid buffer and found that with a cut off of 4 units % in a small study serum acid phosphatase was significantly raised in 11/15 patients with

metastatic PC. The findings were confirmed in later larger studies by Sullivan (1942) and Herbert (1946). It is quite remarkable that this procedure with small variations was the method of choice for the clinical chemical laboratory investigation of PC for over four decades.

Prostatic acid phosphatase

An acid phosphatase fraction (PAP) from prostate tissue was reported by a New York State University research team, with lead author Sidney Schulman in 1964, using radial immunodiffusion. This led to quantitative immunoassays notably by Foti (1977) and Griffiths (1980) using solid phase radioimmunoassay, which showed improved diagnostic accuracy compared to the colorimetric enzyme assays for serum acid phosphatase (SAP). Serum PAP has been assessed and generally regarded as a highly specific but low sensitivity tumour marker, especially in the early stages of PC.

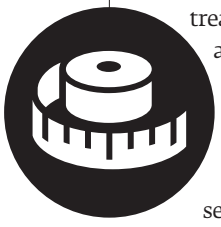
Prostate-specific antigen

The discovery of PSA in human prostate tissue extracts in 1970 is attributed to the American immunologist Richard Ablin, who used gel diffusion precipitation to identify prostatic antigens. It would be a further eight years before PSA was isolated and characterised in human seminal plasma as a potential forensic marker for rape crimes. Progress was achieved a year later at Roswell Park Comprehensive Cancer Center, New York with a research team led by T Ming Chu. PSA was identified and purified in 1979 and shown to be immunologically distinct from PAP. A monospecific antiserum to PSA was produced using tumour extracts as reactive immunogens. After studies using rocket immunoelectrophoresis, a sensitive, sandwich type enzyme immunoassay was developed to measure serum PSA, which was clinically assessed and found to be useful in predictive prognosis, monitoring treatment and the detection of PC recurrence.

The discovery of PSA in human prostate tissue extracts in 1970 is attributed to Richard Ablin

Methods to measure

The Roswell Park cancer research team's patent allowed biotechnology companies to produce PSA test kits from 1986 with FDA approval in the US, leading to their widespread use in the clinical setting. Kits, such as Tandem E PSA employed a solid phase-two site immunoenzymatic sandwich assay with two murine monoclonal antibodies and a chemiluminescent detection of substrate product. Another popular early kit assay was Pros-Check, used conventional radioimmunoassay with a rabbit polyclonal antibody, but results were typically almost twice that of the Tandem E assay. Concerns regarding calibration and reference ranges led to comparison studies, such as Kort and colleagues in 2006 for six automated immunoassay methods were found to show good comparison and close agreement with the WHO 96/ 670 international preparation. The generally accepted reference range for serum total PSA is 0-4ng/ml, but this is now more appropriately age related and of note the upper limit is raised to 6.5ng/ml in men 70-79 years of age.

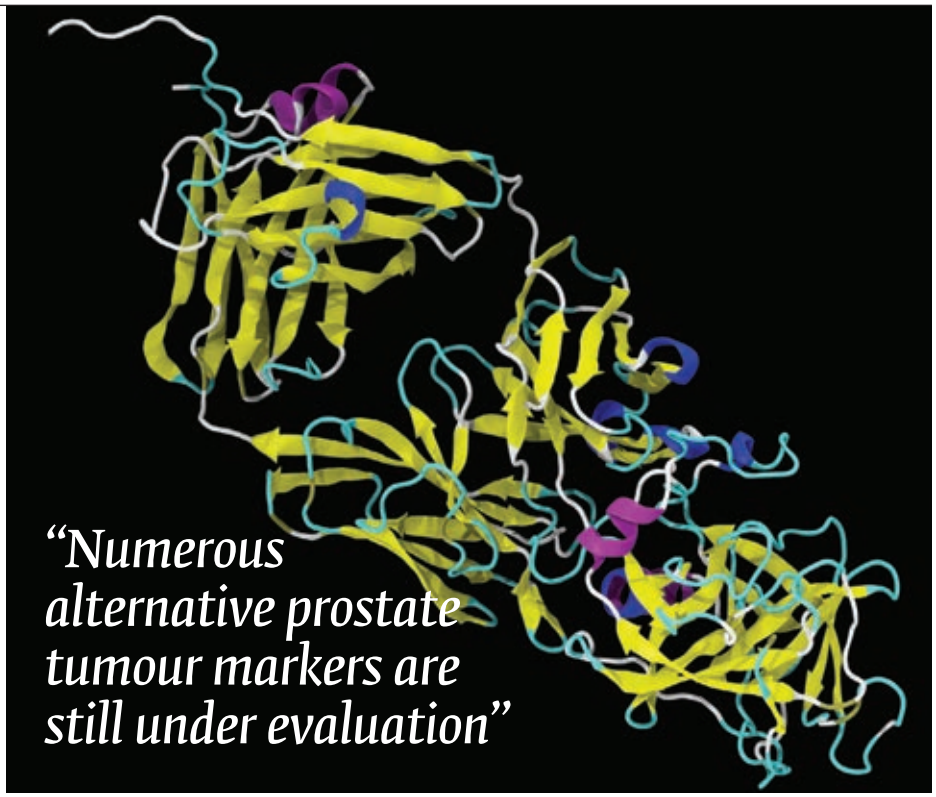


Serum PSA

PSA is now identified as a single chain 33Kda glycoprotein of 237 amino acid residues with 4 carbohydrate side chains. It is an androgen, regulated, serine protease enzyme which is produced by normal prostate luminal epithelial cells. PSA is related to kallikrein serine proteases and can also be identified as hK-3. The main function of PSA is to liquefy the seminal coagulum to promote the release and motility of spermatozoa, some PSA escapes from the prostate and can be found in serum. Various molecular forms exist but PSA is released into blood with around 70% as a stable complex with alpha1 antichymotrypsin (CPSA) and free non-complexed PSA (FPSA) typically constitutes 5-40% of total serum PSA measured. The development of antibodies specific for CPSA and FPSA in 1991 led to immunoassays for each fraction and the use of percentage and ratios.

Clinical use of serum PSA

Serum PSA has several significant limitations as an ideal tumour marker. Levels are also raised in benign prostatic hypertrophy (BPH), prostate inflammation and infection and may be increased in other cancers, notably breast and kidney, and so it is not specific to the prostate. Serum PSA does not always correlate well with the aggressive nature of the tumour, raised results in patients with low grade tumours, which remain localised means treatment may be inappropriate, actually cause harm and affect quality of life. In addition, results are affected by some types of medication, for instance LHRH agonists/antagonists may reduce serum PSA by 50%. Other factors



Right. 3D model of human prostate-specific antigen

include age, race and weight and calibration and performance characteristics of the chosen method of analysis.

Screening

This has been the subject of numerous studies and trials. The 1986 FDA notice recommended serum PSA for monitoring only but with reliable assays available, its use in screening grew rapidly encouraged by observations that a fall in PSA following hormone therapy correlated with response to treatment and that increased results after treatment predicted recurrence. Many large scale clinical studies would take place, however, the chosen parameters often varied, notably in the upper decision limit of the reference range, use of DRE and core biopsies in follow up. It became recognised that patients diagnosed by screening had clinically organ confined disease and around 25% with PSA >4ng/ml were found to have PC on biopsy. Modifications were introduced, including age adjusted ranges, PSA velocity-measures rate of increase, PSA density – prostate size, and the use of free to total PSA %, which was found to be inversely related to the risk of PC.

The contribution of PSA screening in decreasing disease-specific mortality was in doubt due to the conflicting results from two major prospective prostate screening trials, which reported their findings in 2009. *The European randomised study of screening for prostate cancer* (ERSPC) presented data that showed a 20% decrease in the prostate specific mortality rate, while the *Prostate, Lung, Colorectal, and Ovarian Cancer screening trial* demonstrated no significant decrease in prostate specific mortality. Also of great concern was that each study showed that PSA screening led to overdiagnosis and overtreatment with unnecessary biopsies, treatment side effects and stress to the patient. PSA may detect small, low grade and localised tumours which may be clinically insignificant and not require treatment.

Prognosis and recurrence

Research described earlier showed that PSA may be useful in treatment monitoring, risk stratification, predictive prognosis and the detection of tumour recurrence. In 2008, the National Academy of Clinical Biochemistry (NACB) published recommended practice guidelines that PSA is useful for detecting disease recurrence and monitoring therapy and that free PSA is valid to distinguish malignant from BPH when total PSA is <10ng/ml. Numerous alternative prostate tumour markers, such as kallikrein 2 and myeloid protein-14, are still under evaluation. The clinical decision cut off point of <4ng/ml is endorsed by many of the expert panel groups. Irrespective of which type of treatment has been used from active surveillance, surgery, radiotherapy, chemotherapy or anti androgen therapy, regular measurements of serum PSA remain the yardstick for success or failure of treatment.

Active surveillance may involve serial testing of serum PSA every six months, with DRE and an annual biopsy, which, based on results, may lead to treatment. It has also been claimed that a single PSA in early middle age can predict risk of advanced prostate cancer decades in advance, which can help to plan future screening. Expected PSA results following successful TURP (transurethral resection of prostate) at one month are <0.2ng/ml, which requires using an ultrasensitive PSA assay. However, a rise within next 12 months, or a doubling time of six months, indicates progressive disease. The preoperative PSA and the interval between surgery and redetection of PSA by conventional assay can be used to predict disease free survival and pattern of recurrence. Following radiotherapy the decline in PSA is less and lowest level may require at least 12 months, but a rise >2ng/ml over lowest result or three consecutive rises at three and six month intervals tends to indicate radiation failure.

Concluding comments

Despite its controversial role in screening, serum PSA has been the mainstay biochemical marker in prostate cancer for over 30 years. Advances in treatment, such as higher dose radiotherapy, and imaging techniques with increased government funding may improve the outlook for prostate cancer patients. IBMS

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

IMAGE: SCIENCE PHOTO LIBRARY

QIAstat-Dx

The next generation of syndromic insights

QIAstat-Dx® (DiagCORE®) is the next generation of syndromic insights you have been waiting for.

Powered by proven QIAGEN® sample and assay technologies, you can now confidently provide clinical insights to patients with the highest level of versatility.

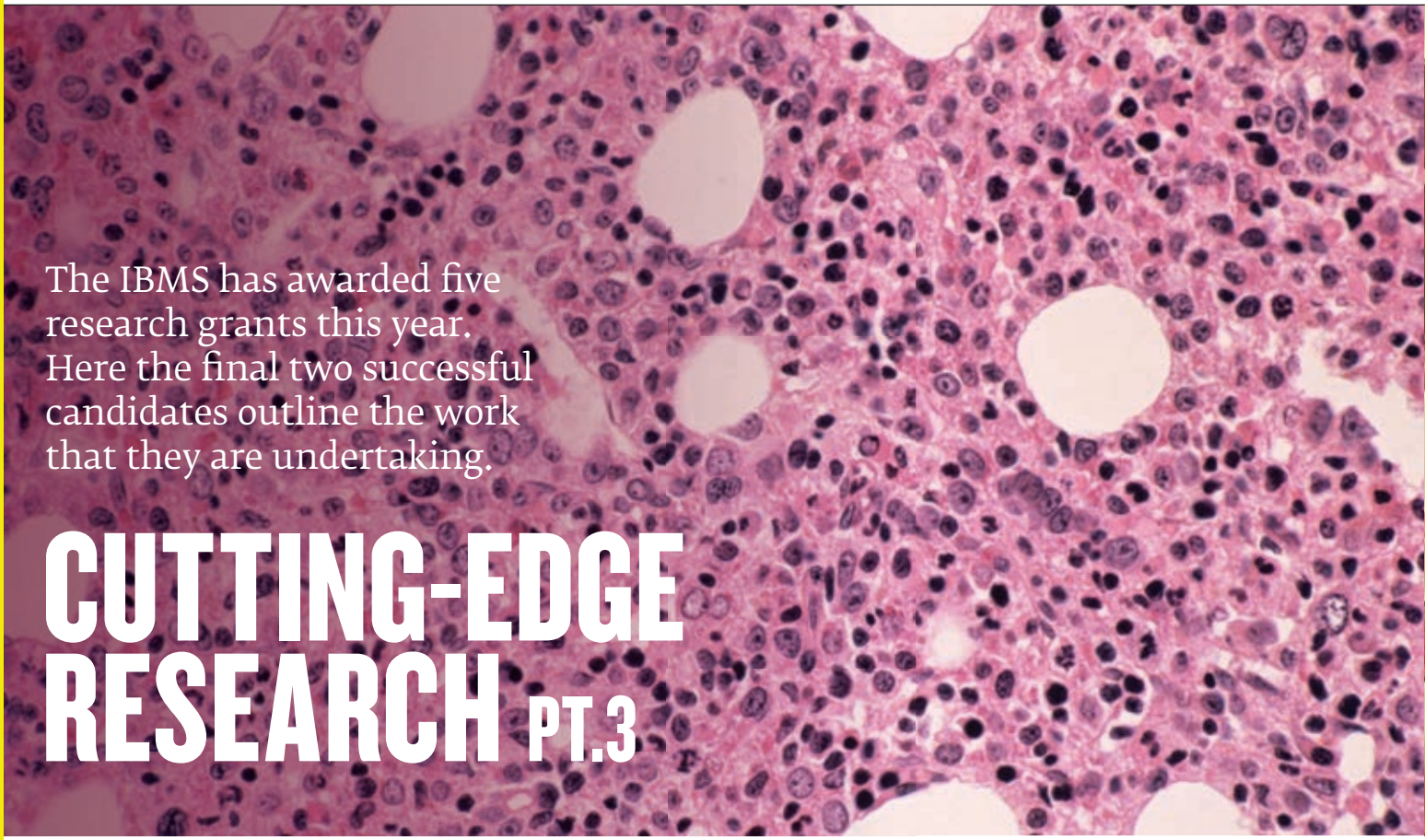
QIAstat-Dx for Upper Respiratory Infections

- Detection of 21 pathogens in about an hour
- Can accept both direct swabs and liquid samples (300 µL)
- Room temperature stable
- Less than a minute hands-on time
- True Sample to Insight solution

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

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

Sample to Insight



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

CUTTING-EDGE RESEARCH PT.3

Steven J Coles

Senior Lecturer in Biochemistry, Head of Worcester Biomedical Research Group, School of Science and the Environment, University of Worcester

Development of a rapid diagnostic test for the stratification of BCAT1 overexpressing acute myeloid leukaemia

Acute myeloid leukaemia (AML) is a rapidly progressing blood cancer that manifests as a block in myeloid cell differentiation and subsequent accumulation of immature myeloid cells (blasts) in the bone marrow. Clinical signs of AML occur as a result of blast accumulation, which leads to progressive bone marrow failure. Based on genetic and clinical manifestations, AML is a heterogeneous disease according to World Health Organization classification.

Gross genetic changes, such as chromosomal translocations, can lead to the development of AML, providing these changes occur in regions of the genome that control blood cell growth and survival (e.g. t[8;21]) (RUNX1-ETO), which mutates the RUNX1 protein, a transcription factor important for normal myeloid cell development.

Recently, the human cytosolic branched-chain amino transferase, encoded by the *BCAT1* gene, has been implicated in the pathogenesis of AML. The canonical function of BCAT1 is to transfer α-amino groups from Leu, Iso and Val to α-ketoglutarate (α-KG) generating glutamate. Studies have shown that the upregulation of BCAT1 in AML cells lowers the intracellular α-KG pool, leading to epigenetic modifications. The effect mediated by BCAT1 is similar to IDH1-mutant AML. As such, BCAT1 upregulation has a negative impact on disease outcome for AML patients.

Currently there is no rapid diagnostic test for detecting BCAT1 upregulation in AML. Therefore, this IBMS Research Grant-supported project aims to develop a point-of-care diagnostic test that will allow the stratification of AML patients according to BCAT1 expression levels.

As BCAT1 may be targeted therapeutically, it is hoped that such a diagnostic test may be clinically informative in the future.

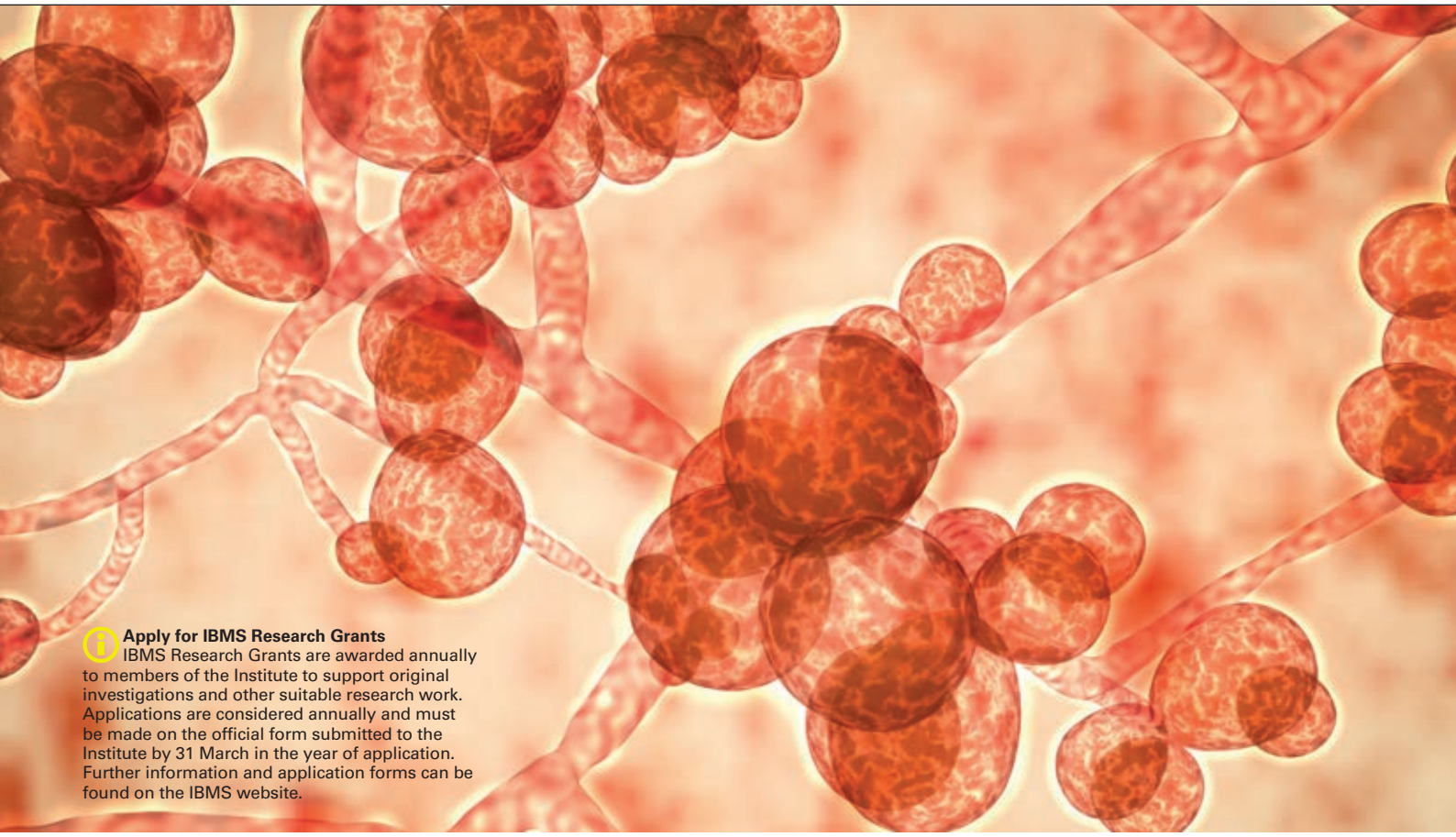
Ucheoma Ugoji

Senior Biomedical Scientist-Section Manager, Barking, Havering and Redbridge University Hospital, London

Engineering and validation of catalytic nucleic acid systems for the effective diagnosis of human pathogenic *Candida* infections

Infections caused by fungi have become a major global problem in hospitals, with the incidence of sepsis caused by fungi increasing since the 1990s. The incidence of *Candida* bloodstream infection in Europe is estimated to range between 6.7 and 54 per 1,000 intensive care unit (ICU) admissions, with a mortality of more than 33.9%. In the UK, a laboratory surveillance conducted by Public Health England in 2016 showed that the overall incidence of candidaemia was 3.6 per 100,000 population. *Candida* infections can become disabling, cause lethal infection and have emerged as the main causes of hospital-acquired nosocomial infection, especially in immunocompromised patients and those hospitalised for long periods of time.

A range of diseases caused by fungal



Apply for IBMS Research Grants
IBMS Research Grants are awarded annually to members of the Institute to support original investigations and other suitable research work. Applications are considered annually and must be made on the official form submitted to the Institute by 31 March in the year of application. Further information and application forms can be found on the IBMS website.

infections that affect healthy immunocompetent individuals generally resolve with chemotherapy, but hospital-acquired infections pose a serious threat to immunocompromised patients on hospital wards and in ICU worldwide. Current diagnosis of fungal infections relies on the isolation and identification of fungi from clinical samples, but such microbiological methods are time-consuming and lack sensitivity. Alternative fast, efficient and cost-effective diagnostic methods are needed urgently. Nucleic acids enzymes are catalytic DNA or RNA sequences that can act as biomarker sensors and molecular switches. Innovative multicomponent multiple nucleic acid enzyme (MNAzyme) systems that can identify DNA biomarkers with high sensitivity and specificity have been developed recently.

These MNAzyme systems offer new opportunities for biomarker detection and multiplexing with the potential to improve on the molecular diagnostic tools currently available. Multicomponent MNAzymes self-assemble and become catalytically active only in the presence of a biomarker target sequence and a hydrolysable fluorescent probe. If a target fungal biomarker is present in a biological sample, detection and quantification of enzymatic amplified fluorescence gives a positive diagnosis.

MNAzymes have advantages for multiplex analysis. The catalytic core and reporter arms are generic and have been designed specifically to perform optimally together without any relation to the target sequence. MNAzymes have a high conformity as they require target-specific binding of two partzymes and two PCR primers, compared to three levels of specificity associated with other multiplex assays. MNAzymes have the ability to discriminate between closely related sequence variants, and this attribute is based on the design of the target sensor arms. MNAzymes also have the ability to discriminate between single base polymorphisms, allowing detection of associated drug resistance.

The system is an improved multiplex PCR design that is specific and requires minimal optimisation.

Despite the advances made in the diagnosis and treatment of candidiasis, the infection still has high mortality rates.

The rapid detection of *Candida* has become very important, especially in immunocompromised patients. Current laboratory diagnostic procedures are time-consuming and require two to four days to identify *Candida* species.

A rapid detection and identification procedure is crucial as *Candida* species infect mostly preterm neonates and immunocompromised patients in ICU. The emergence of multidrug antimicrobial resistance warrants the development of a rapid detection platform for the diagnosis of *Candida* infection. Rapid and sensitive detection of *Candida* infection can play a role in the effective management of candidiasis and treatment monitoring.

This IBMS Research Grant-supported project will develop and implement MNAzymes as simple nucleic acid biosensors for the accurate, fast and reliable diagnosis of human candidiasis. With the use of isothermal DNA amplification, the research aims to develop diagnostic kits that can be used at or near the site of patient care. IBMS

IMAGES: SCIENCE PHOTO LIBRARY

LABORATORY DIAGNOSTIC TEST ENTERS CLINICAL PRACTICE

A blood test that improves the management pre-eclampsia has been introduced into routine practice, write Laboratory Manager **Tim James** and Consultant Obstetrician **Manu Vatish**.

Pre-eclampsia is a serious condition that can affect women in the later stages of pregnancy. While it only occurs in 4% of pregnancies, pre-eclampsia can cause kidney failure, liver failure and seizures. The health of both mothers and babies can be compromised. It is, therefore, important to identify those at risk.

The issue

Until now, there has been no test that can conclusively rule out pre-eclampsia during pregnancy. Consequently, expectant mothers who are suspected of having pre-eclampsia may be admitted to hospital for conservative clinical management and may stay there for several days, while additional testing is undertaken using both ultrasound and laboratory services. This time-consuming process can cause undue stress and anxiety for the mothers-to-be and their families, and will sometimes lead to early induction of labour.

Evidence that the newer markers of pre-eclampsia serum placental growth factor (PlGF) and soluble fms-like tyrosine kinase (sFlt-1) may be of value in its diagnosis have emerged over the last decade. However, studies demonstrating outcome improvements have been limited. To develop evidence that these new markers can be of benefit, a joint project involving the laboratories at Oxford University Hospitals NHS Foundation Trust (OUH) has been conducted over the last three years.

The study

The main study was planned and developed by Dr Manu Vatish, OUH Consultant Obstetrician and Senior Clinical Fellow with the University of Oxford's Nuffield Department of Women's and Reproductive Health, and was funded by Roche Diagnostics. Testing took place at OUH's John Radcliffe Hospital under the guidance of IBMS Fellow Professor Tim James, who is Head Biomedical Scientist and Laboratory Manager in Clinical Biochemistry at OUH.

The biochemistry department's laboratory team measured both PlGF and sFlt-1 in women presenting to obstetrics with clinical symptoms. During pre-eclampsia sFlt rises and PLGF falls and it is thought that the best diagnostic expression of these results is in the form of a single ratio of sFlt:PLGF. The biomedical scientists reported the results and the ratio to clinicians, and were able to demonstrate excellent negative predictive value.

Dr Vatish said: "The stress experienced by mums and their families can be put into context when we see that almost 70% of patients admitted don't actually have pre-eclampsia.

"With this study, and the previous work that has been undertaken, we have shown that we can virtually eliminate all those patients who have no risk of developing pre-eclampsia, allowing us to focus our attention on those with an increased risk."

Tim added: "We gained confidence in the results both through the patient outcomes and analytical performance on the Roche e411 instrument. The value of the study was evident in that clinicians who evaluated the clinical data from the study were wishing to have the service as soon as the study data was assessed. We were able to present the preliminary outcomes to senior hospital staff and were able to present a costs-neutral case for its introduction, which is associated with a significant improvement in patient safety."

Initial method verification work was presented at the 2017 IBMS Congress and staff from Clinical Biochemistry won the best poster competition.

IMAGE: ISTOCK

Routine service for the tests

Following the study, concurrent work streams were undertaken – the development of the clinical protocol for identification and management of pre-eclampsia by the obstetric team, further laboratory verification of method performance and financial assessment of service introduction. The outcome of this work was a routine service for women in Oxfordshire to provide this test as of 1 October 2018. It is now part of the routine repertoire of tests provided by the biochemistry laboratory at Oxford University Hospitals – the first hospital in the UK to provide this.

Tim said: "Historically, our markers of pre-eclampsia have been weak. Therefore, this is a step change in diagnostic accuracy, and provision of this service is the right thing to do for patients.

"We are able to run these tests within a relatively short time frame, and are working towards a turnaround time of 60-90 minutes."

This short timeframe for diagnostic results will allow doctors to rule out pre-eclampsia among patients quickly, and will in turn reduce patient waiting times, free up beds for patients and allow many patients to avoid unnecessary days spent in hospital, possibly unnecessary inducement, as well as easing the anxiety felt by mothers-to-be and their families.

This accuracy of the test has been shared with the Oxford Academic Health Science Network, which is encouraging other laboratories to introduce the service.

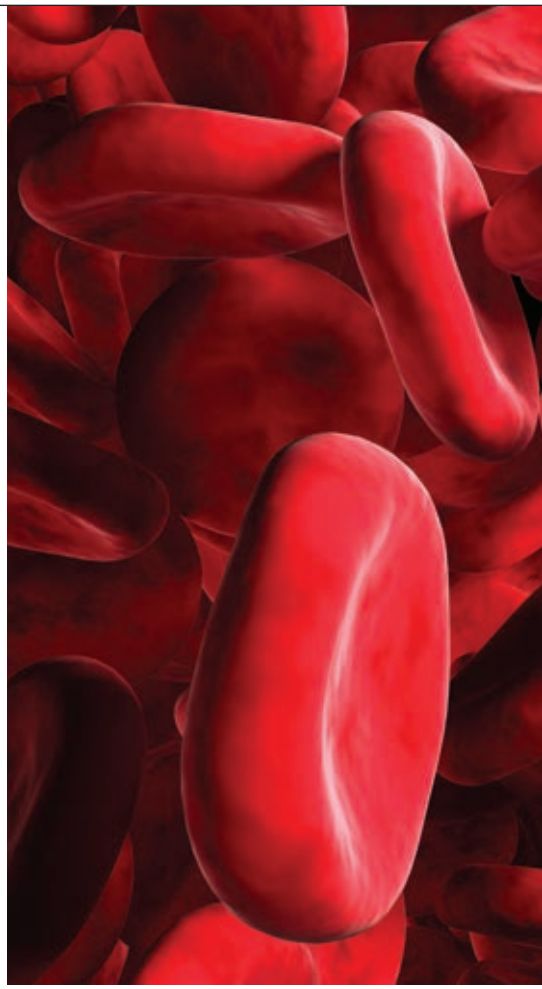
Tim concluded: "The beauty of these tests is that they are not reliant on analysers that are only available in Oxford. The instruments are available at many hospital sites, meaning that the benefits we have demonstrated can be expanded across the UK relatively rapidly and easily, and pregnant women everywhere should be able to benefit. I am aware of a number of other laboratories assessing these tests in the context of trials and studies. I am sure it will be common practice to provide these tests for routine care in the near future." BMS

For more information about the test, visit the OUH website.

"We gained confidence in the results both through the patient outcomes and analytical performance"

HOW TO... ENSURE EFFECTIVE BLOOD STOCK MANAGEMENT

Clare Denison and **Fatts Chowdhury** outline the Blood Stocks Management Scheme and explain how it can reduce wastage and save money.



The Blood Stocks Management Scheme (BSMS) was established in 2001 to understand and improve blood inventory management across the blood supply chain. Hospitals and blood services from England, Wales and Northern Ireland are currently participating in the scheme.

Central to the work is VANESA, a data management system, where hospital and blood service data is collected. In return, participants can view real-time data and charts. The BSMS has a large bank of data on the blood supply chain and detailed knowledge of its various elements.

Participation in the scheme is voluntary and open to all hospitals.

The BSMS collects data from a variety of sources and draws on this data to produce a number of regular and ad-hoc reports. These reports contain analysis and information regarding the various elements of the blood supply chain and inventory management.

Benchmarking

Hospitals that use VANESA can select appropriate categories based on their and other hospitals' profiles to appropriately benchmark their data. This can be done by selecting the size of the hospital (based on their red blood cell (RBC) or platelet (PLT) usage category), their geographical location (based on the Regional Transfusion Committee (RTC)) or clinical specialities available within their hospital.

Once appropriate benchmarking categories have been selected within VANESA, users can view inbuilt tables and charts to compare their data with similar hospitals.

Figure 1 is an example of a line chart. This shows the selected users Issuable Stock Index (ISI) for O D Negative RBCs compared to other hospitals within the same benchmarking cluster

ISI is a calculated field; it gives the user an idea of how much stock they are holding in terms of "days use".

Case study

The NHS has been under huge financial pressures over recent years to provide effective clinical care with limited resources. Blood component wastage is an important financial issue for all hospitals.

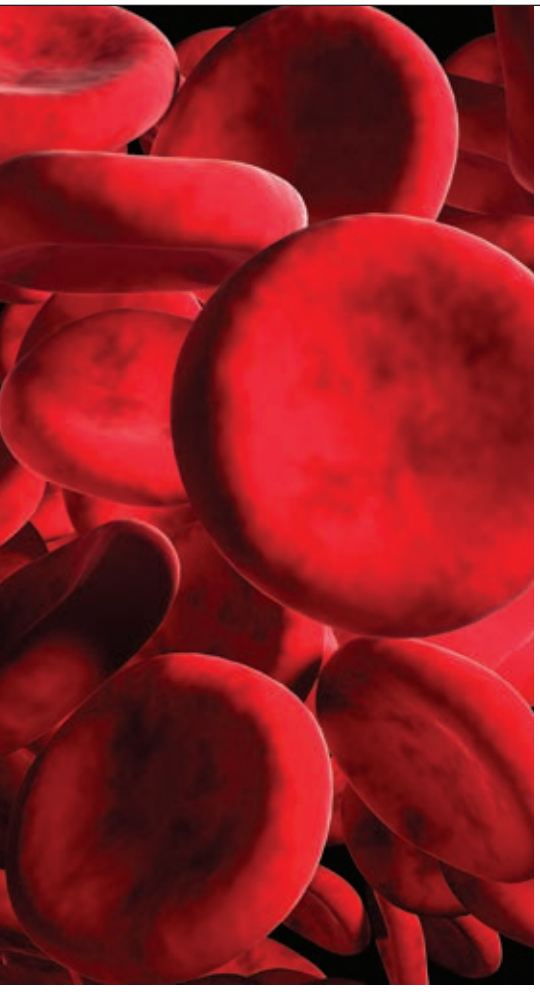
To aid cost savings at St Mary's Hospital, London, which houses specialties which are known to be high users of blood components, the causes and extent of blood wastage within the blood transfusion laboratory were analysed.

The aim was to implement interventions to minimise wastage without compromising patient care while following UK guidelines.

The purpose of the stock review with the BSMS team was to ensure blood stock ordering and stock management is undertaken to minimise wastage from time expiry of RBC units. This was achieved by reviewing the ordering of blood components against regular usage via the blood stock management scheme VANESA system, ensuring that ordering is peer-group-reviewed. This was then followed up with training for biomedical scientists in the transfusion laboratory on how to appropriately order blood components correctly to minimise time expiry wastage.

Previous work by the BSMS has shown a direct link between red cell time expiry wastage and amount of stock held and the age of that stock. Information obtained regarding units wasted due to being out of temperature was used for training targeted clinical teams.

IMAGE: ISTOCK



Results

Comparing data after 10 weeks from implementing the change in stock levels with data for the same months from the previous two years shows a total fall of RBC stock of 42.25%. This equates to a reduction of 68 units in average daily stock holding, which is an £8,500 one-off saving. Revising daily stock ordering based on information from VANESA on the previous two years' data resulted in a reduction of TIMEX units from an average of 43 units to 10 units monthly, which is a potential on-going saving that equates to more than £4,000 per month. Over the first year, savings of £56,500 were made with on-going cost savings of £48,000 per year. Effective blood stock management within the laboratory at St Mary's Hospital has resulted in a reduction of time expired units and a cost saving of over £60,000.

Conclusion

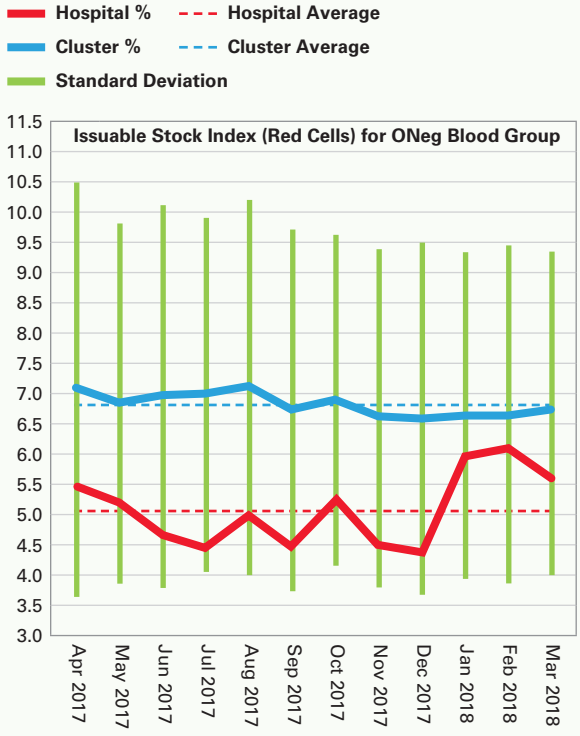
There is a plethora of data held within VANESA that can assist biomedical scientists within hospital transfusion laboratories to review their own laboratories stock holding and amend this based on usage.

This can help to reduce wastage and inappropriate use and therefore create cost savings that can benefit not only the blood transfusion laboratory but also the wider NHS. BMS

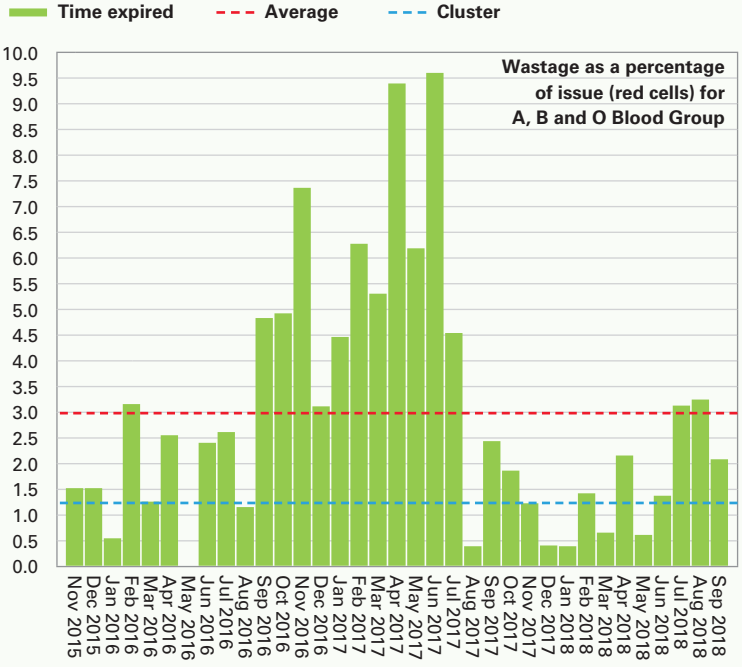
Clare Denison is Lead Specialist for the BSMS, based within NHS Blood and Transplant (NHSBT) and **Fatts Chowdhury** is a Consultant Haematologist with a joint post between NHSBT and Imperial College Healthcare NHS Trust.

For further information, visit **bloodstocks.co.uk**. To see further figures and diagrams to accompany this article, visit **thebiomedicalscientist.net**.

ISSUABLE STOCK INDEX (ISI)



REDUCTION IN TIMEX WASTAGE OF RED BLOOD CELLS FOLLOWING BSMS DATA REVIEW USING VANESA



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ANTIMICROBIAL RESISTANCE UPDATE

After attending a two-day interactive Heralding Education on Antibiotic Resistance (HEAR) course, **Mahrukh Kerawala** and **Rizalea Echaluse** outline the key points.

There is a direct correlation between antimicrobial use and developing antimicrobial resistance. There are major challenges in reducing this threat and although there is no real solution, a rational approach and antimicrobial stewardship efforts are changing behaviour.

The antimicrobial stewardship strategies are: the prudent use of available antibiotics by restriction and preauthorisation, conducting prospective audits, promoting education and public engagement, optimising prescribing practices by de-escalation of therapy, dose optimisation and parenteral to oral conversion.

Microbiology laboratories have contributed to the antimicrobial stewardship efforts by integrating rapid diagnostic and susceptibility testing, laboratory investigation of phenotypic drug resistance and selective reporting, as well as analysis of antibiogram surveillance data. Antimicrobial stewardship has achieved optimal clinical outcome in patients, reduction in antimicrobial resistance and expenditure.

Carbapenem-resistant Enterobacteriaceae

Carbapenemases may confer resistance to all beta-lactam antibiotics. Carbapenemase-producing isolates usually exhibit co-resistance to other

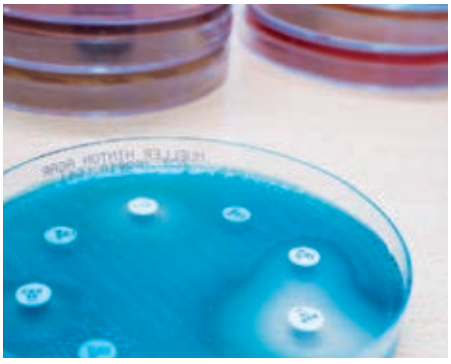

IMAGE: SHUTTERSTOCK

antimicrobials and infections are associated with high mortality rates. The "big five" carbapenemases are: KPC, NDM, VIM, OXA-48 and IMP.

The algorithm for carbapenemase detection, according to EUCAST, is the phenotypic method based on meropenem MIC or disc test followed by synergy testing with boronic acid, cloxacillin, dipicolonic acid and temocillin resistance. The other tests also available are: Gradient strip tests, Carba NP, carbapenem inactivation method (CIM) test, Immunochromatographic test and by matrix-assisted laser desorption ionization – time of flight (MALDI-TOF) mass spectrometry.

Colistin broth micro dilution

Broth microdilution (BMD) is so far the only valid method for colistin testing.

Clinicians are considering colistin as the therapeutic option for the treatment of severe infections caused by multidrug-resistant microorganisms and there is a need to determine the minimal inhibitory concentration (MIC). BMD method (ComASP Colistin) is simple to perform, accurate and is less time consuming. A panel containing colistin in 7 two-fold dilution allows for testing up to four samples. All wells are rehydrated with a standardised microbial suspension. At the end of incubation, observe the growth in the wells and establish the MIC i.e. the lowest concentration of antibiotic that inhibits visible growth.

Synergy testing

Synergy testing is indicated in cystic fibrosis, multiple drug-resistant organisms, or critical infections. MIC test strip synergy applicator system consists of MTS synergy applicator platform and MTS synergy delivery tool to facilitate the operators in performing the tests, therefore increasing the reproducibility. Two strips, each containing one of the antimicrobials of interest, are placed perpendicular to each other, intersecting at the MIC for each antimicrobial when tested alone.

Direct MIC testing

Rapid results and direct specimen, such as blood culture testing, may provide clinicians with therapy guidance and commencing empiric therapy in urgent clinical situations. The results are considered preliminary and should be confirmed by standardised pure isolate testing the next day.

Undiluted positive blood culture is spread evenly onto the chromatic Mueller Hinton (MH) agar plate. MIC test strip (MTS) of the drug is placed on the chromatic MH plate and examined next day for inhibition ellipse. The chromatic MH allows one to discriminate mixed population simultaneously with susceptibility testing. BMS

Mahrukh Kerawala is Lead Healthcare Scientist and Quality manager and **Rizalea Echaluse** is a Biomedical Scientist, both work in microbiology at Health Services Laboratories.
The authors received financial funding from Launch Diagnostics to attend this meeting.

MY IBMS NEWS

AHAWARDS

BIOMEDICAL SCIENTIST OF THE YEAR

The IBMS is sponsoring the Biomedical Scientist of the Year category at this year's Advancing Healthcare Awards (AHAwards).

The award recognises an exceptional biomedical scientist who has used their skills and expertise to advance practice in an innovative and impactful way, making a difference to patients' lives and inspiring those around them.

To apply for this award, nominees must hold HCPC registration and be a practising biomedical scientist based in the UK.

Self-nominations are accepted, and you can also nominate your colleagues or encourage them to nominate themselves.

Nominees for the Biomedical Scientist of the Year must be able to demonstrate leadership and teamwork, measurable achievements and an impact on patient care.

The overall winner in 2018 was Malcolm Robinson, Chief Biomedical Scientist in blood transfusion at Western Sussex NHS Hospitals Foundation Trust, for his Harvey's Gang project. Malcolm was also winner of the Health Services Laboratories Biomedical Scientist of the Year Award 2018 and has gone on to be a winner in the BBC One Show NHS Patients Awards.

The deadline for submissions for 2019 is 14 January and a celebration lunch and awards ceremony will be held on 12 April.

The AHAwards website offers more information about the awards, including a guide on writing a winning entry.

→ **ahpandhsawards.co.uk**

PROFESSIONAL PROMOTION

National Pathology Week

Biomedical scientists and laboratory staff across the UK took part in National Pathology Week.

Throughout the week in November, they informed the public about the profession and its vital role in their healthcare.

National Pathology Week is the Royal College of Pathologists' annual celebration of the profession and is in its tenth year.

IBMS members presented interactive stalls and stands, gave lectures, held quizzes and bake-off competitions, and even opened their laboratory doors to the public.

The IBMS hosted a Twitter chat during the week to discuss public engagement.

It also supported more than 60 members' events to promote biomedical science.

→ **For more information, visit ibms.org/resources**

RENAL PATIENT SUPPORT

WEBSITE LAUNCH FOR SUPPORT GROUP

The Renal Patient Support Group (RPSG) has launched its new website.

It is a non-funded programme that was established in 2009.

The RPSG aims to support patients with Chronic Kidney Disease (CKD), parents and guardians and carers outside routine clinical outpatient appointments at the North Bristol NHS Trust.

The group is evidence-based, recognised internationally, has over 8,000 members and was a finalist for the AHAwards (2018).

The RPSG has 10 key representatives from the UK, UAE, Europe and US.

It has expanded across several social media platforms since it was founded.

→ **For more information on the group, visit rpsg.org.uk**

MELANOMA

PETITION TO BAN SUNBEDS

A petition has been launched in the hope of persuading the government to ban commercial sunbeds in the UK.

If the petition reaches 100,000 signatures then it will be considered for debate in Parliament.

At the time of going to press, it had less than 20,000 signatures and the petition is due to close on 12 January.

The petition says that melanoma kills six people every day and sunbed users have an increased risk of developing skin cancer.

It states: "The NHS is already overstretched. If melanoma spreads through the body, it is notoriously difficult to treat. The treatments that are used are enormously expensive. A sunbed ban would indirectly support the NHS."

Among those behind the call to ban sunbeds is Sandra Phinbow, who is Scientific Advisor to Melanoma UK and is also National Council Member for the IBMS.

She said: "As a biomedical scientist, I am reaching out to each and every one of you to help to bring an end to these avoidable deaths."

The government responded to the petition on 13 November.

It said: "The Department of Health and Social Care takes the risks to health of ultraviolet radiation seriously, including exposure through use of sunbeds."

The statement concluded that it has "no current plans to review policy on sunbeds but will keep the evidence under review".

→ **To view the petition, visit petition.parliament.uk/petitions/223903**

IBMS BRANCH

West Midlands and Birmingham AGM

The West Midlands and Birmingham annual general meeting will be held at 5.30pm on 17 January.

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

There will be a presentation by Hollie Bancroft, an R&D Biomedical Scientist from Heartlands Hospital, entitled "Lessons learnt from the initiation of PEACE at a regional thoracic centre".

There will also be awards for the most improved placement students in BSc Biomedical Science (hons) for local universities.

A light supper will be available and all are welcome to attend the event.

→ **For more information and to book your place, email nigel.coles@nhs.net.**

IMAGES: ISTOCK

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

PRESIDENT'S PRIZE WINNERS

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

UNIVERSITY OF PLYMOUTH

Molly Crawford was awarded the IBMS President's Prize at the recent graduation ceremony at University of Plymouth, having graduated with a BSc (Hons) Healthcare Science degree specialising in Blood Science. Molly completed her degree with integral clinical placements with her honours research project in quality assurance performance in autoimmune diagnostics at Universities Hospitals Plymouth NHS Trust. She has since taken up employment with Conquest Hospital, East Sussex Healthcare NHS Trust in Hastings. Pictured: Molly Crawford along with Malcom Owen (member of the IBMS South West Regional Executive Committee), Dr Craig Donaldson (Head of School of Biomedical Sciences, University of Plymouth), Dr Lynn McCallum (Programme Lead Healthcare Science, University of Plymouth).

UNIVERSITY OF WOLVERHAMPTON

Mohammed Ahmed was awarded the President's Prize at the University of Wolverhampton. Mohammed plans to continue studying at the University of Wolverhampton by undertaking an MSc in Biomedical Science. He is pictured receiving the award from Karen Williams of the IBMS West Midlands Region.

UNIVERSITY OF HULL

Gemma-Kaur-Brown was awarded the President's Prize at the graduation ceremony at the University of Hull. She said she thoroughly enjoyed studying biomedical science, especially the investigation of the properties of microparticles released from pancreatic cancers cells, which she undertook as part of her dissertation. Gemma is looking forward to using the skills and knowledge gained from her degree in her future career.

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

EVENTS AND TRAINING COURSES

DATE	TITLE	VENUE CONTACT
December		
2-4 Dec	**National Osteoporosis Society Conference**	Birmingham I e.gray@nos.org.uk
4-6 Dec	**Three-day update for cervical cytology**	Bristol I SWRCTC@nbt.nhs.uk
5-6 Dec	**Update in cervical cytology – Scottish cytology training school**	Edinburgh I scts@nhslothian.scot.nhs.uk
6 Dec	**Autoimmune IFA event**	Wokingham I jmorrow@menarinidiag.com
7 Dec	**Autoimmune IFA event 2**	Wokingham I jmorrow@menarinidiag.com
11 Dec	**Educational workshops 2018: the ongoing challenges of MRSA**	London I ecarruthers@bsac.org.uk
11 Dec	**Manchester bacteriology discussion group**	Manchester I l.coulthwaite@mmu.ac.uk
12-14 Dec	**BM/cytoscreener update course in gynaecological cytology**	Harrow I LNWH-tr.lrctcbooking@nhs.net
13-14 Dec	**2018 National OPAT Conference**	Birmingham I ecarruthers@bsac.org.uk
17 Dec	**Introduction to blood cell morphology**	Manchester I 01612471485
January		
15 Jan	**Antimicrobial Chemotherapy Conference 2019**	London I ecarruthers@bsac.org.uk
15-17 Jan	**BMS/cytoscreener update course in gynaecological cytology**	Harrow I LNWH-tr.lrctcbooking@nhs.net
21-25 Jan	**Follow-up course in gynaecological cytology**	Harrow I LNWH-tr.lrctcbooking@nhs.net
February		
4 Feb-1 Mar	**Introductory course in gynaecological cytology**	Harrow I LNWH-tr.lrctcbooking@nhs.net

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Sort samples by colour

The BradyJet J2000 Colour Label Printer can print any colour on reliable laboratory sample labels. By setting up a colour code, laboratory specialists will be able to recognise sample categories at a glance. With over 16 million colour variations, users may switch colour every day, or use a different colour per application, storage or urgency type depending on the needs of their laboratory. Next to colour, the BradyJet J2000 also offers 4800 dpi photo quality print to add highly legible data or barcodes a decent scanner could never misread.

Print reliable labels

The BradyJet J2000 prints on Brady's reliable laboratory sample labels that come in matching sizes and shapes for most sample containers including tubes, vials, cryo containers, dishes, plates and general glassware. These labels are designed to stay attached and to remain legible when printed with a Brady printer, even if they are stored in liquid nitrogen and in freezers, or when used in hot water baths or autoclaves. Brady's laboratory sample labels can also resist common laboratory chemicals like acetone, ethanol, toluene, xylene and IPA.

Easy to use

With 26.4 by 38.9 cm dimensions, the BradyJet J2000 has a small footprint and is very practical and easy to use. Spring loaded Brady label rolls can be switched in less than 20 seconds and with automatic label set up, the printer is ready to print in no time. And with up to 101.6 mm per second print speed, even larger colour coded sample labels can quickly be printed on demand.

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HERE TO HELP

COULD YOU BE A SPECIALIST ADVISORY PANEL MEMBER?

Chris Ward, IBMS Head of Examinations, looks at the Institute's advisory panels and how members can play a crucial role.

The eight specialist advisory panels are vital in ensuring the success of the Institute's work. There are advisory panels for cellular pathology, clinical chemistry, cytopathology, haematology, immunology, medical microbiology, transfusion science and virology. Each panel is made up of around 12 "expert" members that include a Chair, Deputy Chair, Chief Examiner, two Deputy Chief Examiners, a Company Member and approximately six "ordinary" members.

Their work includes:

- Organising the scientific programme for their discipline for the IBMS Congress and contributing to other aspects of this major event.
- Working with the Institute on revisions to the existing, and the development of new, professional qualifications, such as the Specialist Portfolios, Diploma of Expert Practice and Higher Specialist Diploma (HSD).
- Representing the Institute on local and national groups and committees.
- Commenting on revisions to Institute professional guidance documents.
- Acting as a source of advice on a range of topics, including patient/service users, emerging technologies and laboratory training.
- Working with the Institute's Education and Professional Standards Committee and other working groups.

Being an advisory panel member gives you the chance to undertake different roles, acquire new skills, develop your network, share and contribute to the development of best practice and to get recognition for your professionalism and expertise in your particular discipline. All of this can help your place of work, as well as your own career progression.

IMAGE: SHUTTERSTOCK

Current vacancies

There is at least one vacancy on each advisory panel for an ordinary member and the cytopathology and virology disciplines are looking for a Deputy Chief Examiner. To be able to join as an ordinary member, you need to have:

- Institute Member or Fellow status
- Scientific or managerial experience in chosen specialty/discipline
- Evidence of liaison with professional and/or academic contacts.
- Chartered Scientist (CSci) status is also desirable, although non-chartered individuals can be appointed initially as a co-opted member, moving to full membership once chartered.

Deputy Chief Examiner applicants can have Senior Fellow of the Higher Education Academy status, rather than CSci status, and should be able demonstrate:

- Academic experience through employment or part-time lecturing
- Experience of setting, marking and monitoring professional exams
- Experience of facilitating or delivering training.

Examiners help to ensure the successful delivery of the HSD by working together to set the exam papers and to mark the portfolios and exams within their chosen discipline and attending the candidate preparation day events. The standard term of appointment for each position on the panel is four years, with the option for further re-appointment. Panel meetings are held twice a year at the IBMS, which will reimburse reasonable expenses. BMS

If you are interested please send a copy of your CV and a supporting letter from your manager to Chris Ward, Head of Examinations at the IBMS. Email: examinations@ibms.org by 7 January.

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Calling All Biomedical Scientists!
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We are looking to recruit enthusiastic HCPC Registered Biomedical Scientists to join our teams in Chemistry or Haematology/Blood Transfusion here at our progressive and forward thinking Trust.

What can we offer you?

You will join our excellent Pathology Service which has full accreditation as a HCPC/IBMS Training Laboratory, ISO 15189 accreditation throughout all Blood Science disciplines and full MHRA compliance for Blood Transfusion. Our ambitious Trust has a good reputation for innovation and now is a great time to join our team as we start to invest in our people, our infrastructure and to develop a new generation of analysers across the whole service coming on line during 2018-19. We encourage applications from both newly qualified Biomedical Scientists with potential for development and those with significant, demonstrable experience. These roles will provide you with the chance to develop your skills within your chosen professional area with generous training and support.

What you can offer us?

You will be enthusiastic, innovative and a great team player. You will also be flexible in your approach and able to participate in the single discipline 24/7 shift system.

Swindon is a great place to live and work with excellent affordable housing opportunities and good local schools. The town is set in beautiful countryside between the Cotswold's to the North and Marlborough Downs to the South. The Pathology Service is based within the modern and well-equipped Great Western Hospital site which is easily accessible from all major routes.

Interested?

Please get in touch to find out more about our exciting opportunities or to arrange an informal visit.

Please contact; **Darren Ames**, Blood Sciences Manager on **01793 607247** or **darrenames@nhs.net**, alternatively contact Ryan Jary, Senior Recruitment Officer on **01793 607975**.

gwh.nhs.uk/jobs

To find out more, please contact
Zoe Blausten on 020 7034 2512

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MY LAB

CELLULAR PATHOLOGY

Consultant Cellular Pathologist **Paul Cross** gives a guided tour of his lab at the Queen Elizabeth Hospital, Gateshead Health NHS Foundation Trust.

I've worked for over 25 years as a Consultant Cellular Pathologist in the department of pathology, based at the Queen Elizabeth Hospital (QEH), Gateshead. When I started, there were three Consultant Cellular Pathologists, now there are 16. This reflects the huge increase in volume and scope of work, but also the move to laboratory consolidation over recent years.

In 2014, the pathology departments from three historically separate local hospitals (South Tyneside Hospital, Sunderland Royal Hospital and the QEH) merged, with the main laboratory being based at the QEH site, with hot labs at the other two sites and mortuaries on all three sites. It serves a population of about 650,000. This consolidation was not without its scientific, political and human issues, but I will not dwell on these as they have been written about previously.

Several years on, I feel privileged to work as a member of the team across pathology as a whole, but in particular my own area of cellular pathology. The pooling of the work from the three hospitals, all historically with different workloads and case mixes, has resulted in a medical and technical workforce with a great range of skills and interests. This means that on a day-to-day basis we can consult with each other and cover most pathological bases.

We work as flexible teams, with areas of interest and identified specialist leads, but have not moved to a formal specialist team reporting structure. This allows us to cross-cover and report across the case mix we have and even during holiday periods we can report without major diagnostic delay.

The surgical workload is about 48,000. We also cover post-mortems on two of the three sites, as well offering a cervical cytology and diagnostic cytology service. Multidisciplinary teams are held on all three sites, and use is made of the hospital shuttle service to ferry staff around, with two bookable electric cars. Cross-site working is essential to maintain links with the clinical teams on the three sites, but does lead to a dearth of pathologists physically in the department at times. The lab itself has about 60 staff, many part-time, to cover all aspects of processing and ancillary testing, both for histology and cytology. Staff are rotated between sections, which helps keep professional skills across the department evenly spread, allows for staff development, but also helps maintain interest. We are now far more heavily automated than ever before, and while water baths and microtomes are still evident, they are partly hidden by machinery more often seen in blood sciences.

We are of, course, part of the overall pathology laboratory, with about 10,000 samples per day arriving across the whole of pathology, across the four main disciplines. A dedicated pathology fleet of courier vans criss-crosses the local area picking up samples and dropping off supplies, and the sheer scale of planning this never ceases to amaze me.

The laboratory has successfully achieved UKAS/ISO accreditation, not bad for what is effectively a new laboratory only some four years old. The whole design principle of the laboratory is flexibility, as work and technology will inevitably change, but in what direction is difficult to fully predict. Whatever does happen, we have, I feel, the ethos and ability to adapt and deliver for many years to come. BMS

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