ONE-TO-ONE

DRUGS RESEARCH

The former government chief drugs advisor Professor David Nutt: *p.16*

HUMAN PARASITES

TRICHROME STAINING

An environmental surveillance pilot study is analysed: *p.38*

MY LAB

CERVICAL SCREENING

A Cytology Manager gives a guided tour of her department: *p.50*

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CONTENTS

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CHANGE FOR CYTOLOGY

The dedicated and passionate workforce deserves the care and respect it gives patients.

I am writing this article fresh from a meeting that the Institute held jointly with the British Association for Cytopathology. The reason for the meeting was to support members in cytology through the extremely difficult and stressful transition from cytology microscopy to HPV testing as the primary test in cervical screening. A consequence of this change will be a reduction of around 80% in the number of laboratories across the UK currently undertaking cervical cytology screening. This in turn means a corresponding reduction in the number of individuals required in cytology.

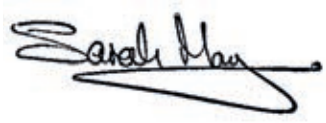
There are many ways to handle change and the provision of open, honest information is usually a good starting point to best enable preparation and planning for that eventuality. By this I mean mental and emotional preparation, as well as the more practical elements of CV updating and evaluation of career options. An enforced career rethink can be as traumatic as bereavement and leave those affected with a similar sense of loss, grief and anger.

Unfortunately, the words "open and honest" have not been associated with this transition and the affected workforce is experiencing all of the uncertainties of job loss or change accompanied by the very real grieving process for a profession that they have loved and, which for many, is about to disappear forever.

Let me be clear, this is not a workforce of Luddites opposed to change or progress, this is a workforce that is dedicated, professional, passionate about their science and one that, I think, has not been afforded the care and respect that they have so fully given to their patients.

Despite the difficult situation, I know this workforce is better equipped than many to adapt or redirect their career according to the opportunities they find; the qualities that make a good cytologist will make them a valuable asset in many other roles. My concern is that there is a lack of joined-up thinking, the value of this workforce is not recognised outside of cytology and consequently good people become disillusioned and will leave our health services. This would be nothing short of a tragedy, particularly in the light of a recent Public Health England consultation that proposed a 10 year workforce strategy. Its basis was that if demand continues to grow at the present rate we will require an additional 190,000 new posts by 2027, but if recruitment continues at the current rate there will be only 72,000 additional staff.

I have just read a PHE screening blog that states "Nurses and doctors carry out cervical screening in primary care". Am I being over sensitive?



Sarah May
Deputy Chief Executive

IBMS

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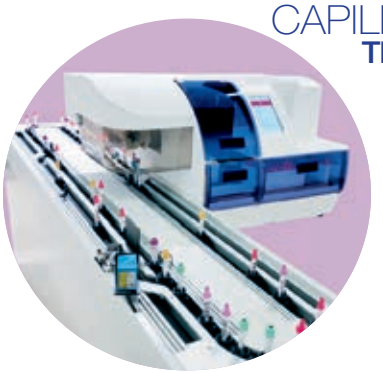

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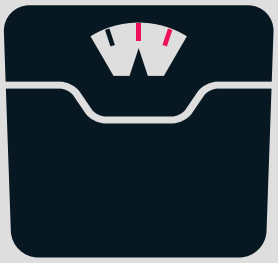
SCIENCE NEWS IN NUMBERS

Primary pupils in England's poorest areas are 4 times more likely to be severely obese than those in the wealthiest.

Overall, the proportion of severely obese Year 6 pupils has **risen from 3.6% in 2009-10 to 4.2% in 2017-18**.



12.5% **In Reception**, in the most deprived areas, **12.5%of children are obese**

5.7% Compared with **5.7% of those in the richest areas**.

The figures come from the **National Child Measurement Programme**.

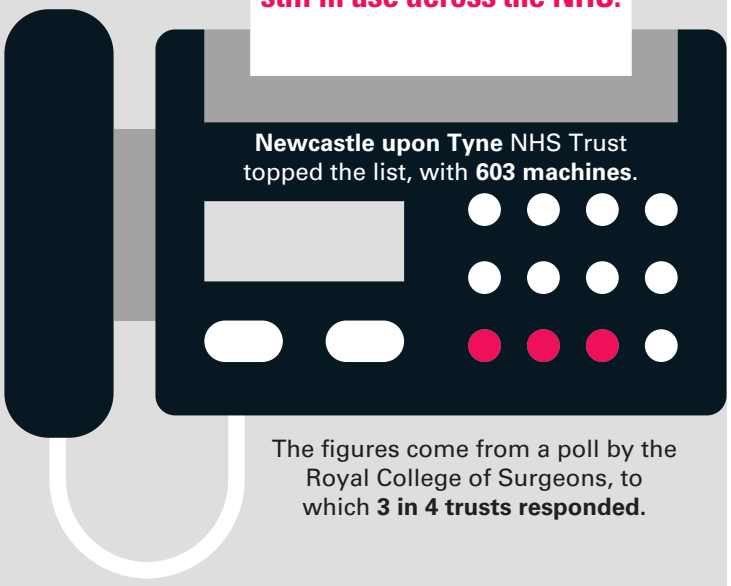
Practising mindfulness meditation for 10 minutes a day improves concentration and the ability to keep information active in one's mind, which is known as **"working memory"**. The claim is based on a study that followed **34 participants** for **8 weeks**.

1/3 **of "gluten-free"foods in restaurants in the US are not actually gluten-free, according to a new study.**

5,600 Based on more than **5,600 gluten tests over 18 months**, the investigators determined that **27%** of gluten-free breakfast meals **actually contained gluten**. At dinner time, this figure hit **34%**.

9,000

There are believed to be nearly 9,000 fax machines still in use across the NHS.



Newcastle upon Tyne NHS Trust topped the list, with **603 machines**.

The figures come from a poll by the Royal College of Surgeons, to which **3 in 4 trusts responded**.

16-24 YEAR-OLDS

The young are turning their backs on booze.

Almost a third of 16- to 24-year-olds in 2015 said they don't drink, compared with around one in five in 2005. **Binge drinking** rates also **decreased, from 27% in 2005 to 18% in 2015**.

SCIENCE NEWS

GENE EDITING

Mouse pups with same-sex parents born

Researchers at the Chinese Academy of Sciences were able to produce healthy mice with two mothers that went on to have normal offspring of their own.

Mice from two fathers were also born, but only survived for a couple of days.

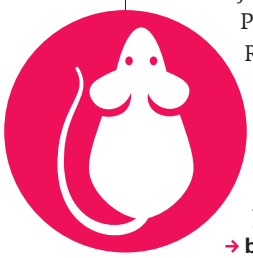
The work, published in *Cell Stem Cell*, looks at why it is so challenging for animals of the same sex to produce offspring and suggests that some barriers can be overcome using stem cells and targeted gene editing.

To produce their healthy bi-maternal mice, the team used haploid embryonic stem cells (ESCs), which contain half the normal number of chromosomes and DNA from only one parent and which the researchers believe were the key to their success.

They created the mice with two mothers by deleting three imprinting regions of the genome from haploid ESCs containing a female parent's DNA and injected them into eggs from another female mouse.

They produced a total of 29 live mice from 210 embryos. The mice were normal, lived to adulthood, and had babies of their own.

→ **bit.ly/BS_NovNews02**



PRION INFECTION

CJD TREATMENT TRIALLED FOR FIRST TIME

In a world first, doctors have been given permission to give a British man with CJD a pioneering treatment.

CJD is a rare but lethal brain disease for which there is no known cure, but the Court of Protection has given permission for the trial use on a human for the first time.

Scientists say lab testing of the man-made antibody has been encouraging, but they admit they do not know how their patient will respond.

The treatment is called PRN100 and aims to prevent abnormal prions from being able to attach themselves to healthy proteins, meaning that they cannot grow and cause devastation throughout the brain.

University College London Hospitals NHS Foundation Trust (UCLH) is set to use it in a patient for the first time after a judge confirmed that it was lawful.

Professor John Collinge, Director of the Medical Research Council Prion Unit at UCLH, who led the development of the treatment, said: "As this is the first time this treatment has been used in humans we cannot predict what the outcome will be, but laboratory testing has shown the potential to treat prion infection."

→ **bit.ly/BS_NovNews01**

HOSPITAL WASTE

NHS WASTE SCANDAL FIRM LOSES CONTRACTS

The Healthcare Environmental Services (HES) has been stripped of its NHS contracts after hundreds of tonnes of waste from hospitals was allowed to pile up at its sites.

Health Minister Stephen Barclay said new arrangements have been made with Mitie to replace the service by HES.

"NHS services continue to operate as normal," he said.

HES says although it did also collect some anatomical waste, it was stored as per guidelines.

The contractor removes the waste from a significant number, but not all, hospitals in England and Scotland.

Mr Barclay said: "While the waste was stored securely, it was not being processed and disposed of within the correct regulatory timescales."

He added: "At no point has there been an impact on public health or any delay to the ability of the NHS to carry out operations."

Garry Pettigrew, HES Managing Director, said his company had been "vilified for providing an excellent service" and problems were due to a shortage of incinerators rather than the company's actions.

IMAGES: ISTOCK/SHUTTERSTOCK

PHOTOACTIVE BACTERIA

LEDs TO TACKLE MRSA?

Researchers are testing whether a simple light-emitting diode (LED) array can be used to inactivate methicillin-resistant *Staphylococcus aureus*, or MRSA.

The photosensitizer, which has been developed at Purdue University in the US is called Ga-PpIX, and is an analog of heme.

Ana Morales-de-Echegaray, the lead graduate research assistant on the project, discovered that Ga-PpIX could be consumed by MRSA strains within seconds, leading to their rapid inactivation using a simple LED array that is safe to use on human skin.

A paper, *Rapid Uptake and Photodynamic Inactivation of Staphylococci by Ga(III)-Protoporphyrin IX*, has been published on the work.

The technology is patented through Purdue Office of Technology Commercialisation, and the researchers are looking for partners to continue developing practical applications for the discovery.

→ **bit.ly/BS_NovNews03**

LASER TECHNOLOGY

NON-INVASIVE BLOOD GLUCOSE TEST

A promising evaluation has been published on new technology to monitor blood glucose levels without needles or a finger prick.

Researchers from the University of Missouri School of Medicine and the Massachusetts Institute of Technology recently evaluated its accuracy.

Early results show that the non-invasive technology measures blood glucose levels as effectively as a finger prick test, without drawing blood.

The study measured the blood glucose levels of 20 healthy, non-diabetic adults prior to drinking a glucose-rich beverage.

Blood glucose levels were then measured in intervals over the next 160 minutes using three methods: spectroscopy, IV blood test and finger prick.

The tests are designed to determine how much glucose remains in the blood and if a patient's insulin-regulating mechanisms are working effectively. The researchers found that spectroscopy predicted glucose values as accurately as a finger prick test.

→ **bit.ly/BS_NovNews04**

WHAT'S HOT AND WHAT'S NOT

HOT

DRIFTWOOD

Nature prescriptions, such as picking up driftwood from a beach, are being offered by GPs in Shetland, to tackle conditions such as high blood pressure and anxiety.

HOT

DYSPRAXIA

In the new series of *Doctor Who*, Tosin Cole plays Ryan Sinclair, the first major fictional character to portray the disability dyspraxia.

HOT

CANNABIS

As of 1 November, doctors have been able to prescribe cannabis products to patients. The new regulations apply to England, Wales, Scotland and Northern Ireland.

NOT

COSMETIC PROCEDURES

A second British woman has died from "Brazilian butt lift" surgery, in which fat is taken from one part of the body and then injected into the buttocks.

NOT

VITAMIN A

Consuming too much vitamin A may decrease bone thickness, leading to weak and fracture-prone bones, according to a new study.

NOT

ERECTILE DYSFUNCTION

For the first time, a team of researchers has found a specific place in the human genome that raises a person's risk of erectile dysfunction.

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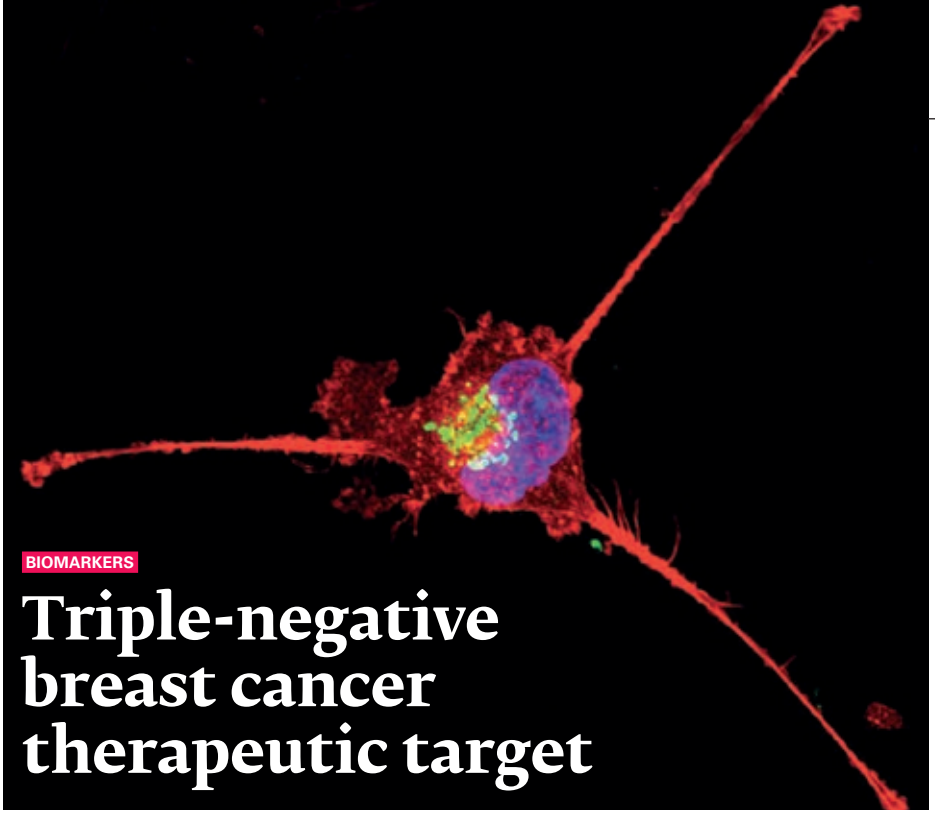

BIOMARKERS

Triple-negative breast cancer therapeutic target

Researchers have previously observed that triple-negative breast cancer (TNBC) patients with higher numbers of myeloid-derived immunosuppressor cells (MDSCs) in their bloodstream had poorer outcomes.

However, until now it wasn't clear how MDSCs are recruited to the primary breast tumour and how they contributed to its progression and spread.

A new report fills in crucial details about the connection between MDSCs and aggressive disease.

Rumela Chakrabarti and colleagues identified a protein, deltaNp63, on tumour cells that directs MDSCs to the tumour and metastatic sites, where they promote tumour growth and metastasis.

Blocking this protein, or the MDSCs themselves, reduced tumour growth and metastasis in a mouse model of TNBC.

Chakrabarti said: "We're excited because we think our findings could make a big difference for triple-negative breast cancer patient. Not only can deltaNp63 be used as a biomarker to help personalise treatment regimens, but targeting it may also provide an additive treatment for triple-negative breast cancer."

→ **bit.ly/BS_NovNews05**

MOLECULAR SIGNATURES

PREDICTING OBESITY-RELATED DISEASE

Scientists have found a new way to use molecular "signatures" from people with obesity to predict risk of developing diabetes and cardiovascular disease.

The research, led by Amalio Telenti at Scripps Research, shows that predictors of future diabetes and cardiovascular disease for a person with obesity can be found among their body's metabolites – molecules that we produce as we live, breathe and eat.

Using cutting edge technologies, the scientists were able to assess the relationship between disease risk and the "metabolome" – a person's collection of hundreds of metabolites, identifying specific signatures that predicted higher risk, according to results published in *Cell Metabolism*.

The researchers found 49 metabolites with a strong association to body mass index – an indicator of obesity.

By looking at these metabolite levels, scientists could predict a person's obesity status with an 80% to 90% accuracy rate.

→ **bit.ly/BS_NovNews06**

UNDER THE MICROSCOPE

This month: Bioelectronic medicine

What is bioelectronic medicine?
It is branch of science that deals with electronic control of physiological function, especially as applied in medicine to compensate for defects of the nervous system.

I think I need a bit more explanation...
Through a convergence of molecular medicine, neuroscience and bioengineering, bioelectronic medicine seeks to develop cures that don't require drugs, or at least rely on them less heavily.

OK, understood. Has this been in the news?
Yes, researchers at Northwestern University and Washington University School of Medicine have developed an implantable, biodegradable wireless device that speeds nerve regeneration and improves the healing of a damaged nerve.

How does it work?
The device delivers regular pulses of electricity to damaged peripheral nerves in rats after a surgical repair process, accelerating the regrowth of nerves in their legs and enhancing the ultimate recovery of muscle strength and control.

Does it have a battery?
No. The device is powered and controlled by a transmitter outside the body that functions much like a mobile phone-charging mat.

Does it just stay in the body?
This is the clever bit – the device, which is size of a penny and the thickness of a sheet of paper, operates wirelessly for about two weeks before naturally absorbing into the body.

Why is that better than a normal implant?
It provides therapy and treatment over a clinically-relevant period of time and directly at the site where it's needed, thereby reducing side effects or risks associated with conventional, permanent implants.

Has this been tested in humans?
No. But while the device has only been tested in rats at present, the scientists say their findings offer promise for a future therapeutic option for nerve injury patients.

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400-010-W-MAX	BioGX **Mycobacterium tuberculosis Complex** - OSR for BD MAX
400-014-A-MAX	BioGX **Pneumocystis jirovecii** - OSR for BD MAX
Meningitis Panels	
400-005-C-MAX	BioGX **Bacterial Meningitis NSH** - OSR for BD Max (N. meningitidis, S. pneumoniae, H. influenzae)
400-006-C-MAX	BioGX **Bacterial Meningitis ELGBS** - OSR for BD Max (E. coli, Listeria spp. Group B Streptococcus)
400-008-C-MAX	BioGX **Viral Meningitis HSV/ VZV** - OSR for BD MAX (HSV 1, HSV 2, VZV)
Bacterial Resistance Panels	
400-007-C-MAX	BioGX **Vancomycin Resistance** - OSR for BD-MAX (vanA, vanB, vanC1, vanC2/3)
400-015-C-MAX	BioGX **Carbapenem Resistance KNO** - OSR for BD Max (KPC, NDM-1, OXA-48)
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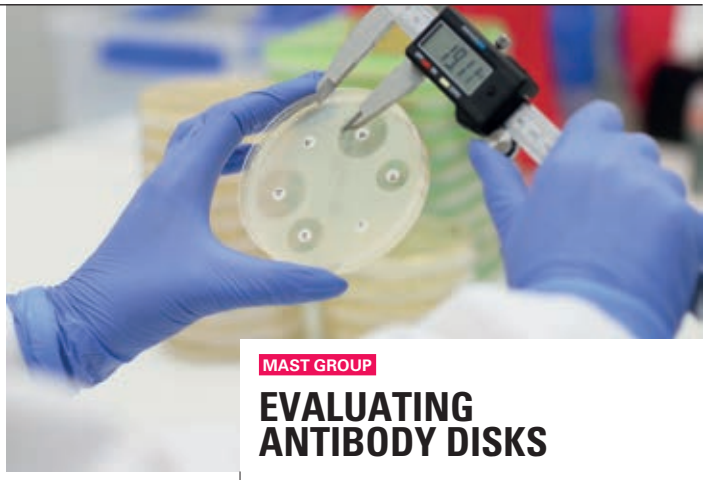


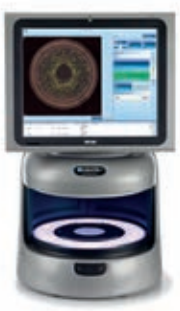
SYNBIOSIS

PROTOCOL 3 AUTOMATED COLONY COUNTER

Synbiosis, a long-established, expert manufacturer of automated microbiological systems, is pleased to announce its ProtoCOL 3 automated colony counter is being used at a major teaching hospital in London.

It is being used to accurately track the spread of carbapenem-resistant bacteria superbugs.

Microbiologists in the infection control group at the hospital are using ProtoCOL 3 to count colonies of carbapenem-resistant and extended-spectrum beta-lactamase producing bacteria, including *E. coli* and *Klebsiella spp.* isolated from patients' stools cultured on a range of different selective and chromogenic plates.



→ **synbiosis.com**

MAST GROUP

EVALUATING ANTIBODY DISKS

EUCAST has evaluated the quality of 16 antimicrobial susceptibility test (AST) discs from nine manufacturers against EUCAST targets and ranges for relevant quality control strains.

Two studies took place to test the AST discs, the first was in 2014, and the second was last year.

A new report highlights that from 2014 to 2017, Mast Group] maintained a high level of consistency of well-calibrated discs, maintaining both quality and performance throughout the studies.

→ **mastgrp.com**

THE BIG QUESTION

THIS MONTH WE ASK

"How could Brexit impact laboratory supply chains and continuity?"

Raymond Gamble

Laboratory Service Manager
Ulster Hospital Laboratories

For the NHS in the UK there remain several unknowns that could potentially impact the service. However, for Northern Ireland there is the added issue of the border between North and South. This is proving a thorny issue and to date nothing has been agreed in relation to the movement of goods and people across this UK/EU frontier.

For laboratories, the main concerns of a "no deal" outcome are twofold; the future timely supply and delivery of goods and services, including replacement parts for equipment; and the potential increase in costs if tariffs are introduced. If these goods need to cross a "hard border" from Ireland into Northern Ireland then there could be further delays in delivery.

Guidance from government bodies to NHS organisations remains confusing; in some cases suggesting there should be no stockpiling of goods and in others saying stockpiling of some goods is appropriate.

It may also present challenges for staff living in Ireland, but working in laboratories in the North and vice versa, if a hard border returns. There is the additional concern that the Mutual Recognition of Professional Qualifications may no longer be maintained, which again may impact the workforce.

The best we can do to prepare is to "plan for the worst and hope for the best".

We are told "nothing is agreed until everything is agreed", so watch this space as all we know for certain is, there is likely to be further change.

IMAGE: ISTOCK

Marie Culliton

Laboratory Manager
The National Maternity Hospital, Dublin

The true answer, at this point, is of course that no one knows. It is dependent on many factors the most important of which is "deal or no deal". Many of the laboratory supply chains are controlled by international conglomerates with headquarters outside the UK. Lean management principles dictate that laboratories implement "just in time" ordering holding minimum inventory. In a "no deal" scenario, the World Trade Organization rules apply, with administrative costs for supplier and customer and expected changes in VAT. The supply chain and tariffs will also be much more complicated if component parts are sourced between EU and non EU countries.

It is unclear if the NHS will address this issue as a whole and move to protect all supply chains, or if this will be left to individual trusts. Large corporations servicing laboratories may already have distribution and logistics infrastructure within the UK. However, some of them service the UK and Irish market from depots in Europe near to the channel.

The situation is not much better for Ireland, which remains in the EU, as many suppliers manage the UK and Ireland market as one operation.

This short piece has just considered the supply chain of reagents, equipment and parts, it has not considered the other crucial supply chains of staff or access to research funding, which will be disrupted.

Like the scouts say "be prepared". The only thing clear at the moment is that nothing is clear.

Angela Jean-François

Divisional Manager Infection and Immunity
North West London Pathology

Pathology labs are no strangers to contingency plans and in the event of a no-deal Brexit, this is n o different. Supply chains are likely to be disrupted, with an anticipated slowdown of the flow of goods. Matt Hancock, Health and Social Care Secretary, has written to suppliers asking for increased commercial buffer stocks, increased national stock holding and plans to use air freight, if ports are blocked.

A resilient supply chain, good communications and close working relationships with suppliers are vital

"THE NUTTY PROFESSOR?"

Professor David Nutt was working for the Labour government when he was forced to resign for his contentious views on drugs. Ten years on, we catch up with him.

Few scientists get to make public announcements on their specialisms, and of those who do, not many will have generated so many column inches in the nation's press as Professor David Nutt.

As a member then head of the government's Advisory Council on the Misuse of Drugs (ACMD) Nutt stirred up a political and media storm in 2007 when he pointed out that, statistically speaking, horse riding was more dangerous than taking ecstasy. That tempest eventually died down, but another blew up in 2009 when he wrote a paper and gave a lecture that argued that drug classification should be based on the evidence of the harm caused. In this scheme of things, alcohol and tobacco ranked higher than LSD, ecstasy and cannabis. Indeed, alcohol was behind only cocaine, heroin, barbiturates and methadone. Cannabis came a lowly tenth. Nutt also said that smoking cannabis carried a "relatively small risk" of psychotic illness.

The outrage was loud. the *Daily Mail* called him "dangerous," *The Sun* dubbed him the "Nutty professor". For Alan Johnson, Home Secretary at the time, it was all too much. Nutt's resignation was the price. "He was asked to go because he cannot be both a government advisor and a campaigner against government policy," wrote Johnson. "As for his comments about horse riding being more dangerous than ecstasy... it is of course a political rather than a scientific point."

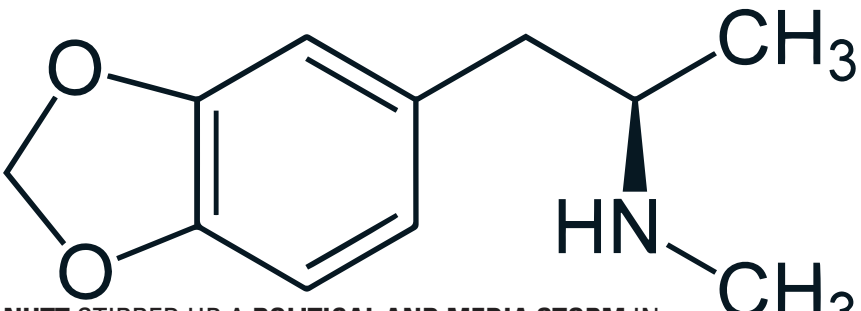
Questioning Nutt's scientific authority didn't go well for Johnson, not when Nutt's career had at that point taken in the Universities of Cambridge, Oxford and Bristol, Imperial College, Guy's Hospital and the US National Institutes of Health. Across all those institutions Nutt's unfaltering "rational, evidence-based approach" had served him well, and he wasn't about to change it to appease anybody, not even the Home Secretary.

"When I heard myself trying to defend

10YRS

"EVEN AS A **RECREATIONAL DRUG [CANNABIS]** IS **WIDELY** USED, AND I AM SURE IT WILL BECOME **LEGAL** IN BRITAIN WITHIN **10 YEARS**,' SAYS NUTT. "I SEE MANY OTHER DRUGS GOING THAT WAY. I THINK IN 100 YEARS' TIME **PEOPLE WILL LOOK BACK** AND WONDER WHAT ALL THE **FUSS** WAS ABOUT."

IMAGES: ISTOCK/SHUTTERSTOCK



NUTT STIRRED UP A **POLITICAL AND MEDIA STORM** IN 2007 WHEN HE POINTED OUT THAT, **STATISTICALLY SPEAKING, HORSE RIDING WAS MORE DANGEROUS THAN TAKING ECSTASY**.

the government's position, I realised I just couldn't," says Nutt today. "It was untenable. I had to say what I said to maintain my credibility as a scientist, because once I lost that I would become an apologist. I gained a reputation, but I don't regret it."

Might just a little more political savvy have preserved his influence at the heart of government? "That is still an open question, though I think the answer is that I probably couldn't have changed things, because my experience during the 10 years I worked with the ACMD, was that politicians are only interested in hearing what they want to hear... in the end they would always rather go with the *Daily Mail*."

"The internet was really taking off at this point so the right of reply was there. I managed to engage an army of sympathisers and was able to bring the debate right out into the open. A lot of people were on my side, and it actually became a fair fight."

Ten years later, it's not an experience he'd care to repeat. "I was younger then. It required a huge amount of effort, writing and talking on the phone day and night. It was physically and emotionally demanding. But in the end I think it changed things, because it became such a public debate. Some people thought I was an idiot, but when they heard the arguments they changed their minds. "

After leaving the ACMD, Nutt set up the Independent Scientific Committee on Drugs, so that he and his colleagues could still bring the scientific evidence to bear on drug policy around the world.

He also remains head of the neuropsychopharmacology unit at Imperial College, where he continues to study the effects of drugs on the brain. "My particular expertise is in giving drugs to patients and volunteers, then measuring what is going on in their brains. The brain is a chemical machine, and drugs are a way of probing what's going on. I have a couple of major research interests at present. In addiction we are exploring new treatments on the basis of brain chemistry abnormality, focusing on the dopamine and endorphin systems. And in depression we are developing a new approach using psychedelic drugs."

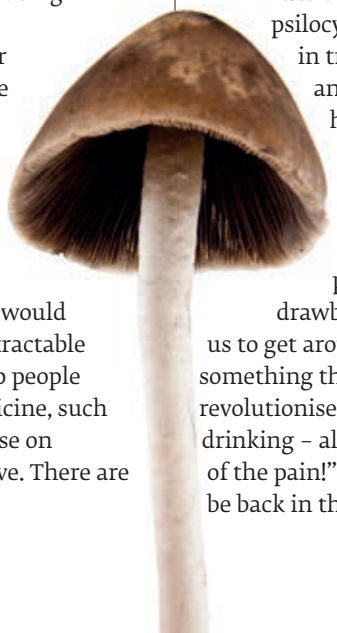
He is also still fighting for medical cannabis to become available. "Hundreds of thousands of people in this country are being forced to break the law. I really want to see an open market for medical cannabis in this country. It would help a lot of people with intractable disorders. It would also help people who are on the wrong medicine, such as opioids. You can't overdose on cannabis, it's not as addictive. There are all sorts of benefits."

PROFESSOR DAVID NUTT

- ✔ **1972** – graduated in medicine from Downing College, Cambridge
- ✔ **1975** – competed training at Guy's Hospital
- ✔ **1978** – Clinical Scientist at Radcliffe Infirmary
- ✔ **1983** – lecturing in psychiatry at Oxford University
- ✔ **1988** – set up the Psychopharmacology Unit at Bristol University
- ✔ **2008** – Professor of neuropsychopharmacology at Imperial College, London.

The ground is already shifting – back in October the home secretary Sajid Javid announced he was changing the Misuse of Drugs Act to allow doctors to prescribe medicine derived from cannabis.

"Even as a recreational drug [cannabis] is widely used, and I am sure it will become legal in Britain within 10 years,' says Nutt. "I see many other drugs going that way. I think in 100 years' time people will look back and wonder what all the fuss was about."



Likewise, he's keen to see the use of psilocybin, or magic mushrooms, in treating psychiatric disorders and even pain. But perhaps his biggest ambition is to produce a safer substitute for alcohol. "I'm working on a synthetic alternative. It's alcohol without all the physical and chemical drawbacks. Modern science allows us to get around those and produce something that is safer and will revolutionise our relationship with drinking – all the pleasure and none of the pain!" And if he succeeds, he'll be back in the headlines yet again. BMS


TOTAL DIGITAL PATHOLOGY

A histopathology lab in Leeds is the first of its kind to go 100% digital. Here we mark the milestone, while **Chloe Lockwood** explains the workflow and **Basharat Hussain** unpicks some of the challenges that were overcome.

The UK has an ageing population. The median age rose by more than six years from 1974 to 2014, and by 2024 there are expected to be more people aged over 65 than under 15.

This means the number of people living with multiple conditions is on the up, as are A&E visits, waiting times and strain across all areas of the NHS.

With 70% of medical diagnoses based on work carried out by biomedical scientists, it was inevitable that build up would result in pressure exerted on pathology departments.

A recent Royal College of Pathologists (RCPath) report says pathology requests are increasing by nearly 5% every year. In September, the college revealed a workforce census shows that only 3% of NHS histopathology departments have enough staff to meet clinical demand.

"The cost of staff shortages across histopathology departments is high for both patients and for our health services. For patients, it means worrying delays in diagnosis and treatment," says Professor Jo Martin, RCPath President. "Making sure pathology services can cope with current and future demand is essential if we are to ensure early diagnosis and improve outcomes for patients,"

Among the report recommendations are "better IT for day-to-day work" and "capital investment to implement digital pathology more widely, so staff can work more efficiently and flexibly".

It is against this backdrop that last month Leeds Teaching Hospitals NHS Trust and the University of Leeds announced a major milestone – a histopathology department that is now 100% digital.

The department, located in St James' Hospital in Leeds, is one of the largest in

the UK, processing over 1,000 pathology slides a day, and it is now digitally scanning every slide.

The step-by-step process that each slide goes through has been rigorously tested and received ISO15189 accreditation, laying the foundations for national guidelines on using digital pathology.

Dr Darren Treanor, Consultant Pathologist at Leeds Teaching Hospitals NHS Trust and University of Leeds, says: "The way we are digitising pathology services in Leeds enables us to produce the quality images pathologists need to diagnose patients quickly and safely. Going digital not only allows the pathologists to do their work on a computer, but it also unlocks the possibility of using the computer to help make the diagnosis, offering huge potential for the future."

Traditional methods present challenges, including transportation of slides, storage, and sharing of information with other pathologists for a second opinion. But through digital pathology, these challenges can be side-stepped.

The technology is hoped to speed up and improve diagnosis and, in the future, may help to detect small areas of cancer that have spread to lymph nodes, improve quantify and rapidly direct pathologists to areas of abnormality in the tissue sample.

To date, 200,000 slides from patients at Leeds Hospitals have been digitally scanned using technology developed by its diagnostics partner Leica Biosystems.

In addition, there is an archive of 386,000 anonymised digital slides (the largest collection in the country) housed by the University of Leeds for research and teaching.

"Demand for pathology services will continue to increase, and digital pathology has the potential to improve workflow and pool resources across hospitals to help improve the patient experience," says Basharat Hussain Programme Manager at Leeds Teaching Hospitals NHS Trust.

CHLOE LOCKWOOD

Biomedical Scientist Lead for Digital Pathology at Leeds Teaching Hospitals NHS Trust explains the move to digital pathology.

Digital pathology unlocks major potential to transform laboratory services, and enhance the role of the biomedical scientist with the developments in AI. Most importantly, the digitising of the histopathology laboratory service has the potential to improve patient safety and reduce the time it takes for a patient to receive their result.

As part of the digital pathology project at Leeds, I had the role of Leadership and Management Fellow in Digital Pathology, and I have been the lead on implementing a full digital pathology workflow into the laboratory. There are many aspects to consider when going digital, but my main focuses were: laboratory workflow and efficiency, working with the laboratory staff before, during and after the implementation, and accreditation.

I have been fortunate to present my work at the Digital Pathology Congress in London and was awarded the Chief Scientific Officer's Healthcare Science Rising Star award for the work I have done on the project.

A huge change

The laboratory is scanning around 1,000 slides a day, which equates to 250,000 slides every year. It's important to recognise that going digital is a huge change management project, and isn't easy. The key to implementing digital pathology is in the details, and it is the laboratory staff who will make it succeed or fail. It is vital that lab staff are involved at every step, and they should feel empowered and engaged to make the changes necessary to make implementation successful.

Digital pathology is also a fantastic tool, which can be used to train biomedical scientist staff in histological techniques, and demonstrate and explain process artefacts so they can enhance the quality of their work.

Scanning slides also gives biomedical science staff the opportunity to learn a new skill. As part of the project, I created a full training and competency programme, and, at present, we have 17 members of staff who are fully trained. The aim is to ensure every member of staff receives training in digital pathology.

Workflow

Digital pathology is a great way to establish collaborations and we are working with Leica Biosystems on the project. It is also a fantastic opportunity to work with other healthcare scientists in the trust. We worked closely with medical physics colleagues on choosing the appropriate monitors so that pathologists could make a confident diagnosis.

It is vital to work with colleagues in IT, as there are so many factors to consider that require their input, such as storage, infrastructure and integration. The option to share knowledge and expertise is invaluable.

Implementing digital pathology is a good opportunity to streamline the entire laboratory workflow to make it more

200,000

A DIGITAL SLIDE IS AN IMAGE CREATED BY THE COMPLETE DIGITISATION OF THE GLASS SLIDE AT UP TO 200,000 DOTS PER INCH (DPI). IF PRINTED AT A STANDARD 300 DPI, THE IMAGE WOULD BE THE SAME SIZE AS A TENNIS COURT

efficient. Looking at the laboratory workflow from start to finish can identify areas that can be leaner, and eventually absorb the additional time and free up the resources required to scan slides. A good example is slide archiving and retrieval, and MDT preparation. Pathologists can have instant access to an image for an MDT, instead of waiting for the glass slide to be retrieved from file. This has a direct effect on lab staff who file slides, as their time can be used more efficiently for other tasks in the lab. It also has benefits for the multidisciplinary team meetings, and more time can be spent discussing individual patient's needs just by transitioning from glass to digital.

Improving diagnosis

The most important aspect of all the work that has been done is patient safety and benefit. In September 2018, the Leeds histopathology laboratory gained ISO15189 accreditation, with digital pathology for primary diagnosis included – the first NHS laboratory of its kind. I prepared and submitted the evidence for the laboratory validation and verification of the laboratory workflow. Having accreditation is a way of assuring staff and patients that the services that are provided are safe.

With digitising glass comes the opportunity to automate processes. This can reduce the number of patient misidentification errors and avoid the limitations of glass and paper in terms of transport, storage, and management. Digital images are safely and securely stored and backed up, so that there is minimum risk of losing an image. It also means faster referrals and second opinions, and the time a patient is waiting to receive their result and deciding on next steps can be significantly reduced.

There is still a long way to go, but advancements such as AI are becoming more of a reality. AI could support pathologists to improve diagnosis, and it could also allow biomedical science staff to take a more active role in patient diagnosis by screening cases before allocating them to pathologists.

I am proud to be on this multidisciplinary journey and I hope I can inspire people to take their own; both for themselves and for the benefits it will ultimately have for patients.

BASHARAT HUSSAIN

Programme Manager at Leeds Teaching Hospitals NHS Trust

Basharat looks at three key learnings from the transformation: location of the scanners, tracking/bar code system, looking at the long-term goals for the team.

Decide the best location for the scanners in the lab

When we embarked on this project, we visited other laboratories in Europe to learn from their experiences and to see how they implemented digital scanning. What was interesting was that most laboratories had a separate scanning room where the scanners were housed.

Bench space is often at a premium in pathology labs, but we felt that locating the scanners in a different room would not help our efficiency. In our view, every glass slide would have to travel further distance, delaying the process and increasing the risk of breaking or losing slides.

Working with the lab staff we did an options appraisal, considering 10 different options for where the scanners could be located, shortlisting them and then assessing the time required for each option. The outcome was that we wanted the scanners to be part of the lab and, together with the staff, we were able to find ways to create the space needed and make the scanners part of the laboratory environment. Once in place, we ran a competition with staff to find a way to name the scanners – the winner was Harry Potter characters – which helped to connect the technology to the human side of the lab process.

Implement a barcode system

The pilot we undertook for digital scanning involved 150 slides a day and we used a manual system to follow the slides progress and input information to match each slide to a patient. This worked for the pilot, but when we considered scaling this up to over a thousand slides a day it was not practical. The administrative burden of inputting that amount of information and risk of error made a manual approach impossible. Automation is crucial if you are to successfully scale the process.

A major part of the transformation, therefore, was to implement a barcode tracking system that is integrated into the reporting system and allows each slide to be followed through the pathology lab process with a single barcode, scanned at each stage of the process. This presented a significant IT challenge, as a number of pieces of equipment in the lab were controlled by standalone computers, which were not connected to the network and often running older operating systems. We had to upgrade various IT platforms and work with different suppliers involved in running the lab to accommodate this approach.

The benefits were significant – time is now saved by having a barcode added to each slide just once, and used throughout the process, and the chance of error is significantly reduced. It is also easier to identify where a patient's slide is at any stage of the process, which is helpful when pathologists need to get their hands on a tissue sample urgently.

Help teams to understand the long-term benefit

Digitally scanning slides adds another stage to the pathology lab process – and, while it takes only two to four minutes to scan a slide, doing this at scale can add to the time a slide is in the lab. In addition, you are adding a new stage to a process that has existed with little change for many years.

The key is for the whole team to understand the long-term goal of digitally scanning slides. The benefits of digital pathology in improving the workflow for pathologists, being able to change slides and views at the touch of a mouse, rather than swapping glass slides in and out of a microscope, and the portable nature of the images means that time could be saved at the diagnosis stage when the images reach the pathologist.

We have six pathologists who diagnose digitally, for neurological and breast cancer. They report that using digital images reduces the time it takes them to assess the slide and make their diagnosis. Over the next few months we will be building confidence and validating pathologists in other specialities to diagnose digitally. This will give us the opportunity to assess the time taken for the end-to-end process, from tissue to diagnosis.

The journey to scanning every slide we produce has helped us to find more efficient ways of working and, while we have added another stage to the process, it is with the aim of unlocking the huge potential that digital scanning offers to the diagnosis of cancer. That is something we can all be proud of. BMS

DIGITAL PATHOLOGY FAST FACTS

The file size of each digital slide is 1gb – about **300 times the size** of the average photo you take on a smart phone.

It takes up to four minutes (dependent on amount of tissue on slide) to scan a slide digitally to this level of resolution (**40 times the size** they are in real life).

A Leica Biosystems Aperio AT2 scanner can scan **400 glass slides in one cycle** and can work overnight to **digitise the images.**

Over 1,000 slides are **prepared and scanned in Leeds** every day. This creates **1 terabyte** of new data per day.

If you were to lay all the glass slides produced in Leeds histopathology department in one month, **end to end**, it would stretch for a **mile**.

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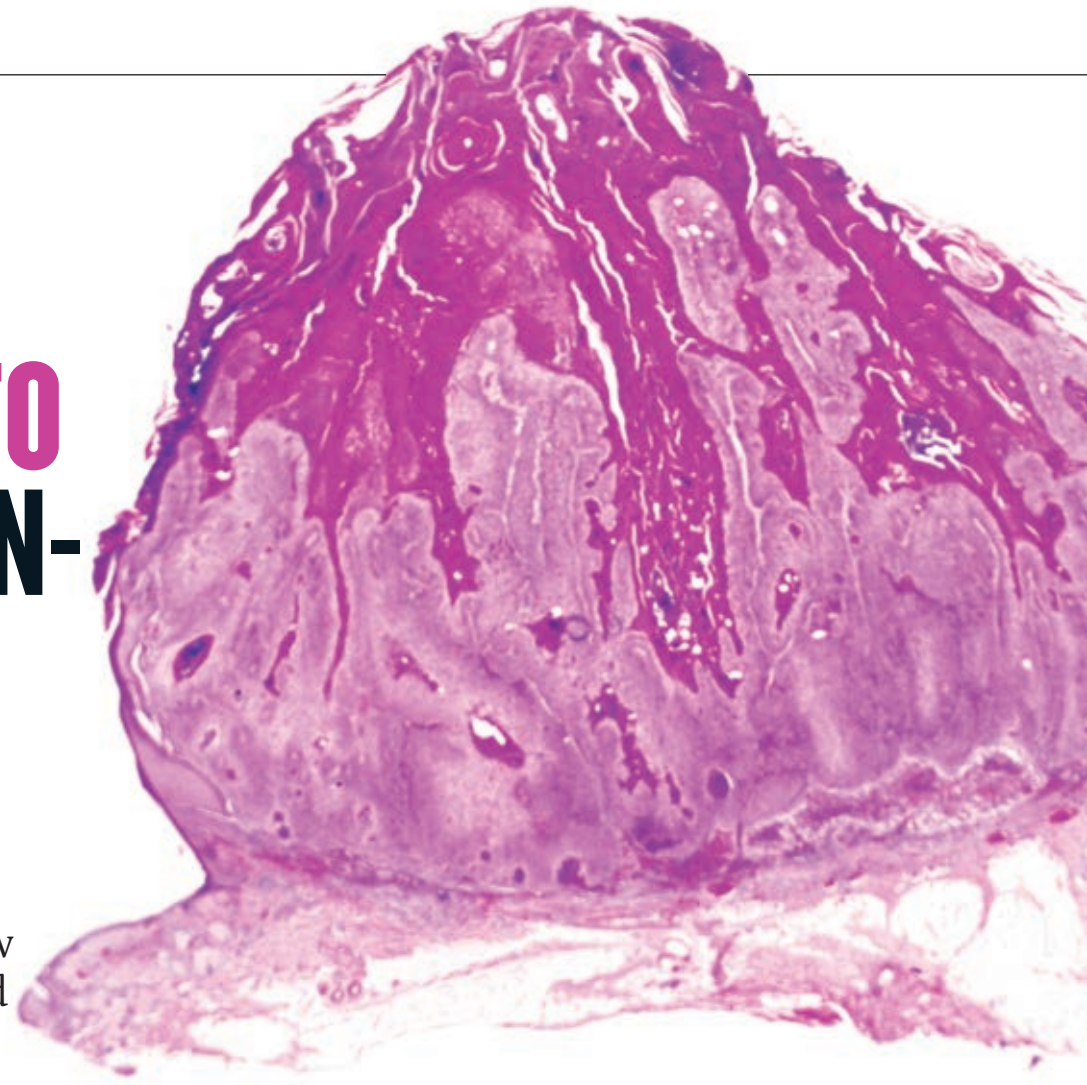


A GUIDE TO FERGUSON-SMITH DISEASE

What is Ferguson-Smith disease and how can it be distinguished from cutaneous squamous cell carcinoma? Chartered Scientist **Jakub Jawny** discusses his research.

Ferguson Smith disease (FSD) is an extremely rare inherited skin condition, clinically and histologically almost indistinguishable from cutaneous squamous cell carcinoma (cSCC). The gene responsible for this autosomal dominant condition was mapped to 9q22-q31 and subsequently mutations in the gene responsible were discovered in transforming growth factor beta receptor 1 (TGFBR-1). Patients typically endure years of multiple enlarging cutaneous tumours, usually on the head and neck (H&N) and on the extremities, which spontaneously resolve within months leaving deep-seated scars and don't appear to have the capacity for metastasis.

Making a positive diagnosis of an FSD-related tumour is problematic as there is considerable overlap with cSCC and keratoacanthoma (KA). Identification of FSD from biopsy interpretation alone is almost impossible. How can the pathologist approach these cases? Are there any features from the clinical history and histology that may allow us to make a presumptive diagnosis of FSD, which should alert the clinician to take a detailed family history and carry out genetic testing to rule out this rare genetic condition?

A project was developed to examine various factors, including detailed study of clinical and histopathological features of skin tumours in FSD patients with a comparison with cSCC. Retrospective slide review of 40 FSD and 40 cSCC cases was performed. cSCC were divided into cSCC LR (low risk) and cSCC HR (high risk) using defined histological criteria.

Clinical clues

It would appear that over 72% of the cutaneous tumours occur on the H&N, in particular on ears, nose, mouth and lips. A quarter of all tumours appeared on the limbs. The trunk and anogenital region were rarely affected. Tumours on the extremities tended to be much bigger, up to 7cm in diameter in comparison with those on the H&N (2-5cm). The tumours appear as reddish macules, which become larger and ulcerate to form a horny plug which eventually self-resolves to leave a deep scar. The resolving tumours are characterised by areas of immune-mediated inflammation and fibrosis.

Possible precursor lesion

In our study, we potentially identified three phases of evolution (precursor/follicle, invasive and regression) in biopsies of FSD and many of the cases showed multiple phases in one biopsy. It would appear that we could identify a potential precursor lesion where we observed follicular plugging and epidermal expansion in the overlying and adjacent epidermis close to the invasive tumours (Figure 1).

In 15% of FSD cases, an epidermal/follicle phase was found in comparison with 5% and 0% of cSCC HR and cSCC LR,

IMAGE: SCIENCE PHOTO LIBRARY

respectively. This is a potentially interesting finding as recently keratoacanthomas and some SCC (follicular/infundibular subtype) are thought to be derived from the hair follicle rather than surface epidermis.

Proliferative phase

Using Scottish Intercollegiate Guidelines Network (SIGN) data set for the reporting of squamous carcinomas, further analysis of cases was performed to assess a presence of histological features, which may confer a HR subtype. Knowing that FSD tended not to metastasise we expected the FSD tumours to show only LR features, but unexpectedly HR features were observed in FSD patients.

Deep invasion beyond the epidermis into subcutaneous fat was found in 32.5 % of FSD cases. Perineural invasion (which is associated with local recurrence in cSCC) was seen 15% and vascular invasion in 5%. In comparison, cSCC HR group had 20%, 20% and 5% of these features present respectively. Statistical analysis also showed the highest median of HR features in cSCC HR of 3.0 following by 1.5 in FSD and 0 in cSCC LR.

Regression

In this stage, invasive elements were infiltrated by an immune cell infiltrate. Here the tumour was under attack from macrophage giant cells with evidence of cell damage to the squamous tumour cells, which left keratin debris (inflammatory regression). Other areas showed more advanced changes of established regression or fibrotic evolution. Histology showed zones of fibrosis, loss or drop out of tumour cells and immune response to keratin.

Established regression was found in 10% of FSD cases and only in 5% in LR cSCC but not observed in HR cSCC.

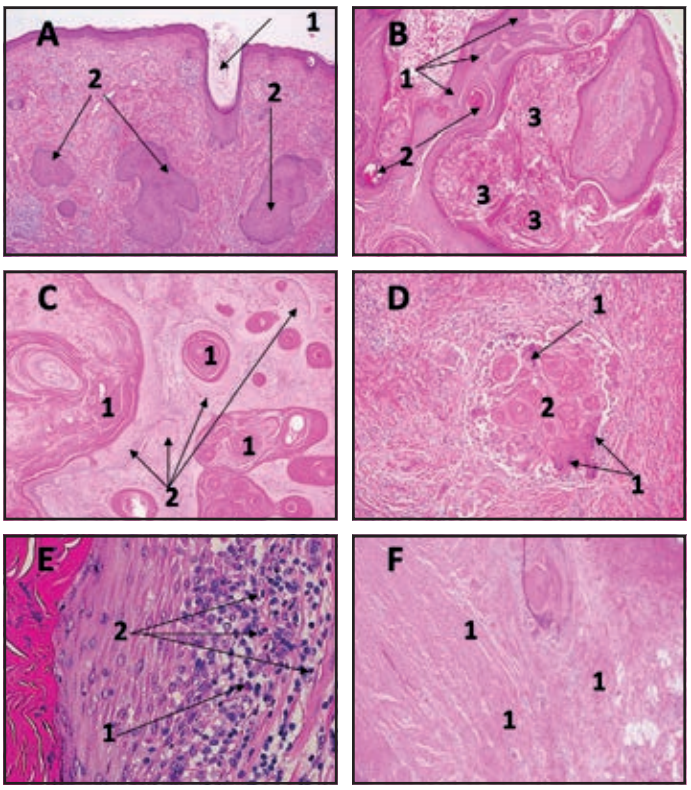
Pathology diagnosis

FSD is associated with a high number of lesions (average 20.5 per patient). This should be the very first clue to a potential diagnosis. Also, the study has identical criteria which, although they cannot provide a definite FSD diagnosis, should alert the reporting pathologist to the possibility of an underlying genetic mutation of FSD. These include precursor lesions in the hair follicle, multiple stages of evolution (particularly all in one biopsy) including KA-like areas, well differentiation and areas of inflammatory and established regression. Finally, and quite unexpectedly, the study also showed that HR features such as PNI and VASI do not exclude a diagnosis of FSD, as previously suspected.

Therapeutic model

The project is a preliminary study into the features of FSD and needs to be corroborated by further larger studies, but shows some potential areas of interest. FSD tumours undergo spontaneous involution and regression. The mechanisms involved in these processes may provide extremely important clues to the molecular pathway involved in tumour progression and involution. This knowledge and understanding could help in the discovery of pathways which could be manipulated by targeted therapy in patients with advance and metastatic cSCC. This could potentially be accomplished by stimulating activation of the molecular and immunological pathways in halting and reversing the proliferation of tumour cells. BMS

Jakub Jawny is a Chartered Scientist from Queen Elizabeth University Hospital (QEUH), Glasgow. This article was written with QEUH Consultant Histopathologist **Colin Moyes**, and **Adrian Pierotti**, a Senior Lecturer at Glasgow Caledonian University.



Left. The stages of FSD tumour progression and evolution. **A** is a precursor lesion (Epidermal Stage 1) with mild follicular plugging **(1)** and epidermal expansion **(2)**. In **B**, KA-like lesion (Stage 2), a collar of epithelium is seen **(1)** with a horn cyst **(2)** and the plug, which is filled with keratin **(3)**. Follicular pattern of invasion (Stage 3) in Figure **C** with central cystic **(1)** and with peripheral squamous epithelium **(2)** are present. **D** and **E** are Inflammatory regression pattern (Stage 4), with macrophage giant cells (2D-1) and with keratin debris (2D-2). In **F** there is Fibrotic involution (Stage 5) with collagen deposition **(1)**. HE stain, 200x.

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The Amplidiag® Easy (Mobidiag UK) is an automated system for nucleic acid extraction and PCR set up for moderate to high throughput volume screening of gastrointestinal pathogens and antibiotic resistances directly from stool samples. The Leicester Royal Infirmary (LRI) has recently evaluated the system. "We were attracted to evaluating the Amplidiag® Easy as a way to modernise our enteric laboratory, with a streamlined molecular multiplex screening approach, to simplify workflow and improve turnaround time of our enteric samples," states Dr Chris Holmes, Clinical Scientist at LRI, who led the evaluation.

Testing for multiple enteric pathogens using conventional culturing methods is known to be time consuming and carries an ever-present risk of missing clinically important pathogens, such as non-0157 verotoxigenic *Escherichia coli*. "Another appealing feature is the Amplidiag® Easy's ability to run several different panels to screen for most major enteric bacterial, viral and parasitic pathogens, or combinations, with the option of screening for carbapenem and colistin resistance genes," Chris Holmes continues.

Multiplex PCR can also increase the speed of testing samples and reporting of negative results, allowing clinicians to make earlier decisions on patient management. For example, with faster results the wards can react quicker to prevent potential outbreaks by moving positive patients into isolated side rooms. Likewise, patients that are not

infected can potentially be discharged sooner. Quicker diagnoses may also allow earlier tailoring of antibiotics, thus reducing the cost and time of prescriptions, but most importantly it will improve patient outcomes.

In the case of LRI, the use of automated sample processing could free up biomedical scientists to work up the more critical positive samples while the automated instrument works in the background. Paul Bird, Trainee Clinical Scientist, who performed much of the practical work, states: "During the evaluation we found the Amplidiag® Easy to be very user friendly due to its simple instructions and easy to follow software on the touch screen monitor. The touch screen set up gives a step-by-step process for adding all reagents, consumables and samples making loading simple." Chris Holmes sums up the evaluation: "The results showed comparable performance to routine methods with the benefit of detecting additional pathogens that are not covered by these routine methods. We are confident that this machine could be installed into any laboratory and workers of all ability and experience, even those with little molecular diagnostic experience, could load, run, extract and maintain the machine with minimal training."

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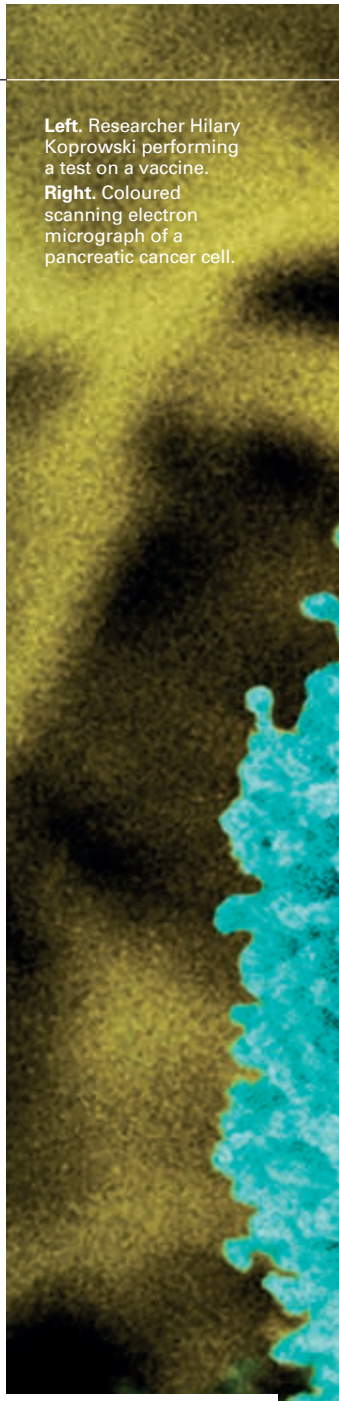

Left. Researcher Hilary Koprowski performing a test on a vaccine.
Right. Coloured scanning electron micrograph of a pancreatic cancer cell.

CLINICAL CHEMISTRY CLASSICS: TUMOUR MARKERS

The series on tumour markers continues with a brief review of pioneering work in the development, analysis and clinical application of an important serum tumour marker- CA19-9.

CA19-9 tumour marker

The existence of a pancreatic tumour associated antigen was first demonstrated by a research team in Philadelphia, Pennsylvania, led by the noted Polish immunologist Hilary Koprowski in 1981. Although colon cancer was their main interest, by coincidence it was also observed that the antigen was present in patients with pancreas carcinoma. The antigen was characterised by this group combined with a research team led by John Magnani at NIH, Maryland in 1982.

Two monoclonal antibodies 19-9 and 52a were produced by hybridomas obtained from a mouse immunised with human colon carcinoma cell line SW 1116. Separation techniques used included autoradiography, immunostaining of thin layer chromatograms, solid phase radioimmunoassay and GC/MS. The 19-9 antigen was found to be a high molecular weight glycoprotein mucin in serum shed from normal epithelia of the pancreas, gall bladder or gastrointestinal tract but overexpressed in pancreatic cancer and several other malignancies. Interestingly, the mucin also contains the sialylated blood group Lewis-a epitope lacto-N-fucopentaose II. It is estimated that around 6% of Caucasians and 22% of Africans lack the Lewis antigen and are unable to produce CA19-9. It has been proposed that CA19-9 binds an adhesion molecule on vascular epithelia promoting metastasis.

Pancreatic cancer

Around 10,000 people are diagnosed with pancreatic cancer (PC) each year in the UK, with only 21% surviving 12 months and a poor five-year survival rate of just 5%. It is disheartening that there has been no significant improvement in these figures for the last 40 years, despite improvements in surgery, imaging and chemotherapy. It is sometimes called "the silent killer", due to the lack of specific early clinical symptoms and suitable

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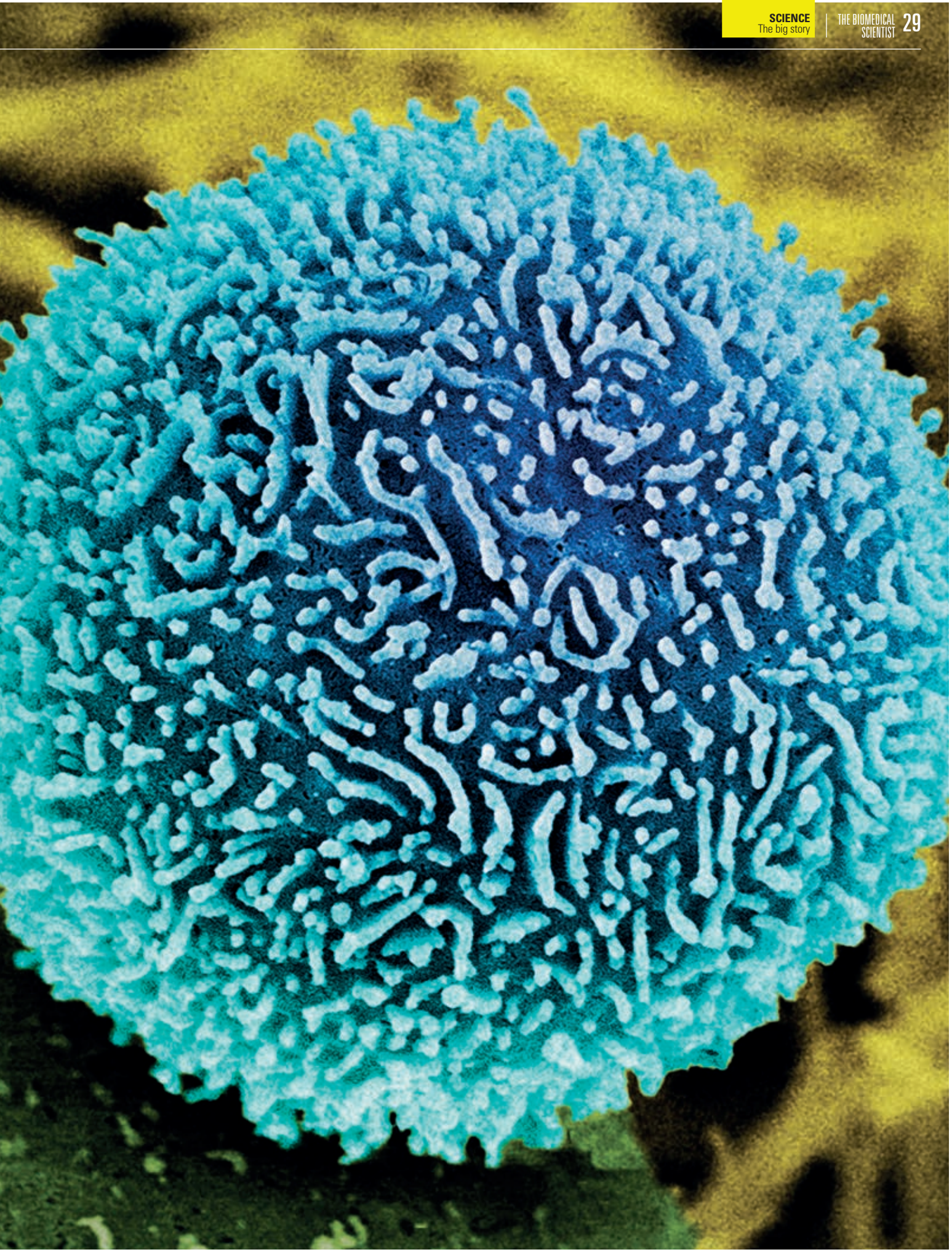

"There is a raised public awareness, with media articles of clinical trials and treatment options"

screening tests for an early diagnosis, and it has been proposed that micro-metastatic invasion precedes tumour formation. This may explain why 80% of patients are diagnosed late, with only 20% eligible for surgery. A total of 95% of patients have ductal adenocarcinoma, with the majority of primary tumours located in neck or head of pancreas. A biopsy taken with endoscopic ultrasound and fine needle aspiration and histology can determine staging and cancer cell type of the four main pancreatic neoplasms, which affects treatment options and likely prognosis. US expert panels in 2016 recommended chemotherapy pre-surgery for operable cases, and for metastatic PC multi-agent chemotherapy or, more recently, multimodality treatment combining cytotoxic agents such as gemcitabine with immunotherapy to harness T cell immunity and reduce inflammation associated with a poor prognosis.

Serum CA19-9

This is the most studied and clinically useful biomarker for PC, based on the results of numerous clinical trials and their interpretation by meta-analysis data. The university-based research on CA19-9 led to the foundation of Centocor, a biotechnology company that developed a number of immunoassay types commencing with a solid phase radioimmunoassay in 1983. It was claimed the assay was simple to perform, required 0.1ml serum and established a reference range of 0-37units/ml now universally accepted. In a small study of 80 patients with PC, 79% exceeded the upper limit and most had results between 400 and 192,000 units/ml. The studies that followed tended to focus on assay specificity from other pancreatic disorders and the potential for use of CA19-9 in population screening. A study by R Farini and colleagues in 1985 showed serum CA19-9 was able to discriminate PC and chronic pancreatitis, which is the most common confounding diagnosis on presentation. A landmark treatise by W Steinberg in 1990 examined the results of 24 studies and found the assay had a specificity of 90% and sensitivity of 80%, was of value in assessing suitability of patients for resection and help prognosticate survival, and claimed CA19-9 was the "gold standard" marker for PC. However, it was soon recognised that elevated serum results also occur in biliary tract obstruction, inflammatory bowel disease, pancreatitis, cirrhosis of liver and certain other malignancies. CA19-9 has been evaluated in at least two large screening studies of asymptomatic populations, by T Homma and R Tsuchiya in Japan (1991) and JE Kim in South Korea (2004), both concluded that screening was ineffective because of a very low positive predictive value. During the 1990s, improved CA19-9 assays were developed using automated immunoassays with chemiluminescent detection by companies such as Roche, Abbott, and Fujirebio of Japan. The emphasis for clinical value during the last 20 years has been based on CA19-9 in prognosis. N Maisey and colleagues from the Royal Marsden Hospital reported in 2005 that serum CA19-9 was an independent prognostic factor in patients with inoperable PC on systemic chemotherapy (including gemcitabine). A Harvard study a year later by Cristina Ferrone and colleagues claimed that perioperative levels of serum CA19-9 can predict stage and survival in patients with resectable PC. The prognostic and predictive value were confirmed in more recent reports in an Australian study led by JL Humphris in 2012 and in the US by Katherine Poruk in 2013.

Concluding comments

Many alternative biomarkers have been assessed – including CEA, CA50, PAM (anti MUC1) elastase 1 and osteopontin – however, CA19-9 remains superior, despite the limitations described, which appears common to the CA series of markers as illustrated in previous articles on CA125 and CA15-3 and this may be related to their epithelial origin and common structures.

Possible alternatives include genetic micro-array testing, proteome protein profiles and microRNA patterns in pancreatic juice, saliva and blood. There is also a considerable optimistic literature on preventative approaches by identifying risk factors which may damage DNA leading to mutations in PC, including tobacco smoking, diabetes, family history of PC, pancreatitis, obesity, heavy alcohol consumption and several inherited syndromes.

There is a raised public awareness with media articles of clinical trials and treatment options and the deaths due to PC of high profile figures such as Patrick Swayze, Steve Jobs, Luciano Pavarotti and most recently Aretha Franklin. IBMS

Stephen Clarke is a retired IBMS Fellow.

To see the references, view the article online at **thebiomedicalscientist.net**.

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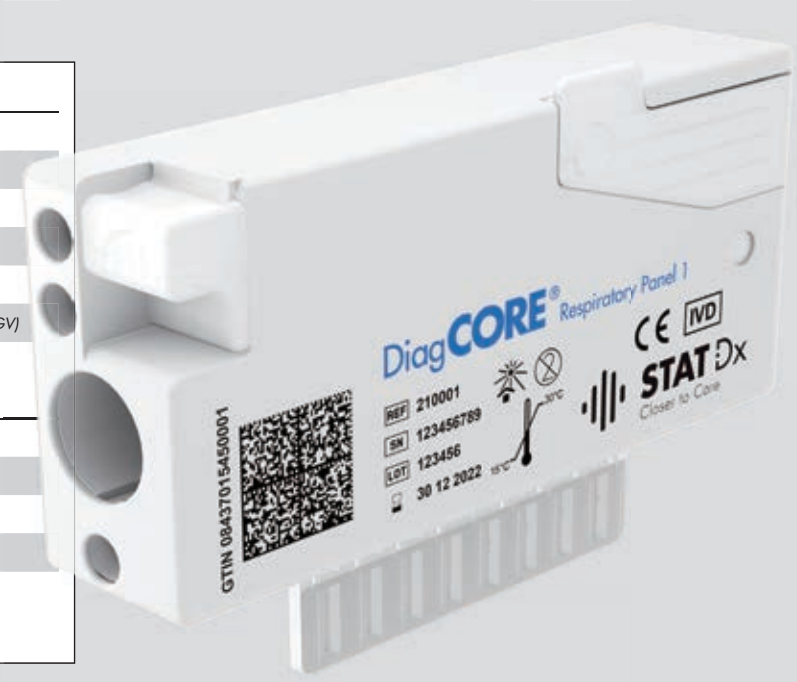
Enteropathogenic E. coli (EPEC)	*Norovirus GII*
Enterotoxigenic E. coli (ETEC) lt/st	*Rotavirus A*
Campylobacter spp. (C.jejuni, C.upsaliensis, C.coli)	*Sapovirus (GI, GII, GIV, GV)*
Plesiomonas shigelloides	
Salmonella spp.	**Parasitic**
Shiga-like toxin producing E.coli (STEC) stx1/stx2	*Cryptosporidium spp.*
Shiga-like toxin producing E.coli (STEC) O157:H7	*Cyclospora cayetanensis*
Vibrio cholerae	*Entamoeba histolytica*
Vibrio parahaemolyticus	*Giardia lamblia*
Vibrio vulnificus	
Yersinia enterocolitica	



*QIAstat-Dx coming soon, currently available as DiagCORE.
DiagCORE is intended for in vitro diagnostic use in Europe.

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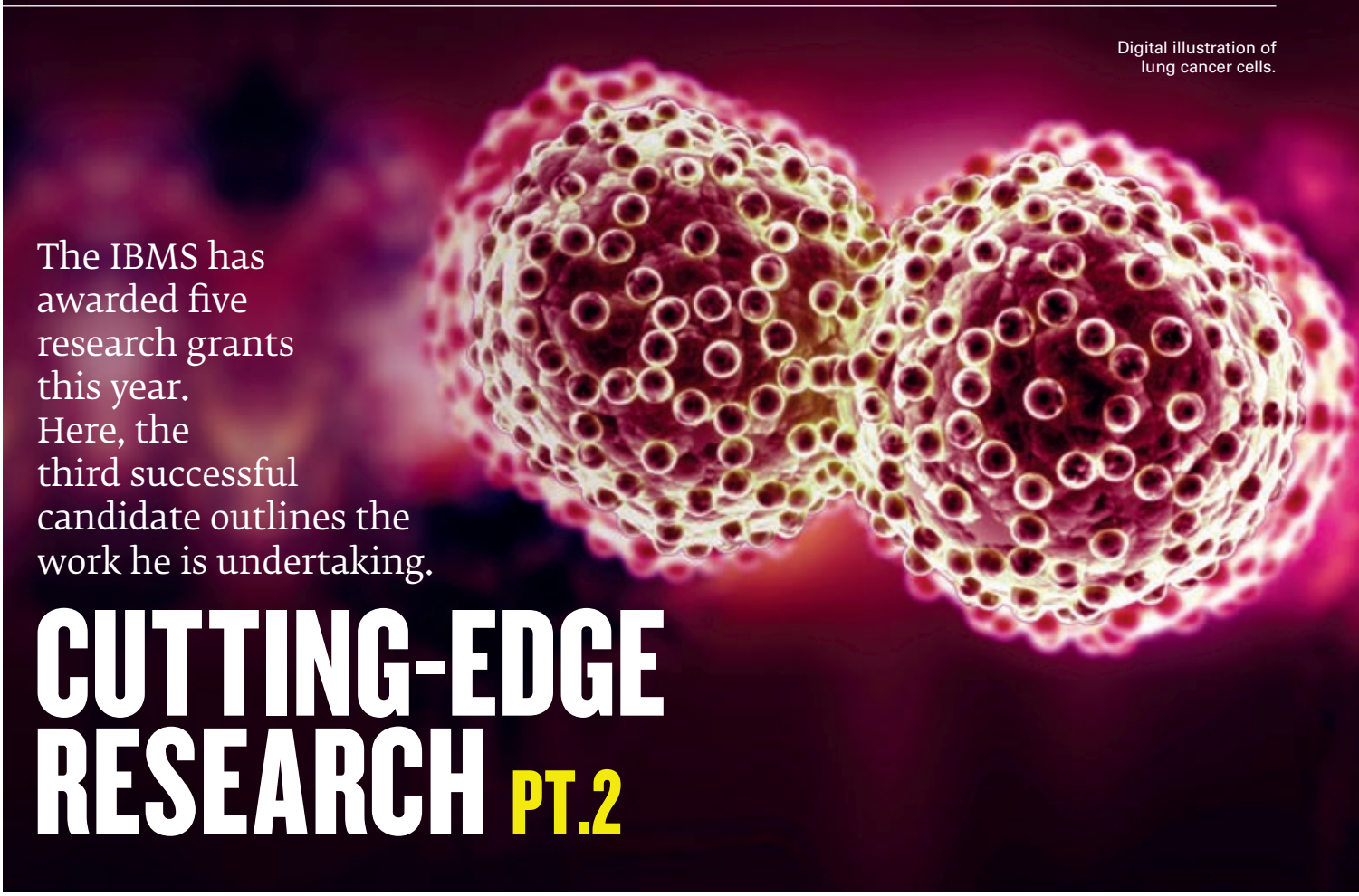


Digital illustration of lung cancer cells.

The IBMS has awarded five research grants this year. Here, the third successful candidate outlines the work he is undertaking.

CUTTING-EDGE RESEARCH PT.2

Rotimi Ajayi

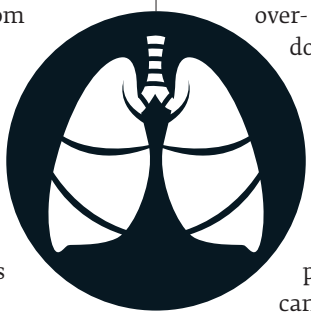
Specialist biomedical scientist in cellular pathology, Royal Papworth Hospital NHS Foundation Trust

Histopathological assessment of alternative fixation protocols for simulated tumour fine-needle aspirates in resected lung cancer

Lung cancer is a major cause of death worldwide and a leading cause of cancer mortality in the UK, accounting for one in five of all cancer deaths. Long-term survival is poor, as most patients present with advanced disease, and less than 25% of individuals are deemed suitable for surgical resection. Evolving knowledge of lung cancer requires an improved protocol for the downstream molecular analysis, as it determines the choice of therapy, accurate restaging following neo-adjuvant therapy and prognosis.

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive but highly effective procedure to investigate radiologically suspicious lymph nodes in the chest. Since its introduction, EBUS-TBNA has emerged as the gold-standard approach to diagnose and stage lung cancer, and is also a useful diagnostic approach for a number of other respiratory conditions.

Given the wide clinical use of EBUS-TBNA to investigate lung cancer, laboratory technical staff and pathologists have to perform an increasing number of complex tests on small and sometimes poorly cellular samples. Critically, as most patients present with inoperable lung cancer, EBUS-TBNA is often the only tumour material available from patients with advanced disease. In these patients, much hope is being placed upon the identification of driver mutations in genes, such as *EGFR* and *ALK*, to improve survival with targeted therapies in patients with inoperable disease.



Essential for these processes is the extraction of high-quality and high-yield DNA and RNA.

At present, pathology laboratories rely on the widespread use of formalin for fixation of tissues. While cost-effective and acceptable for most existing laboratory tests, formalin is highly detrimental for DNA and RNA preservation. Current methods for sample fixation are rapidly becoming the rate-limiting step in the development and uptake of techniques for tumour molecular analysis. Formaldehyde-based fixatives preserve morphology but chemically modify bio-molecules, and over- or under-fixation can affect downstream applications.

The aims of this research grant-funded study are to explore and quantify the benefits of formalin-free PAXgene processing and develop protocols for handling lung cancer specimen. BMS

IMAGES: SHUTTERSTOCK/ISTOCK

Autoimmunity in Focus

Rachael Winwood, Biomedical Scientist in Immunology at Sandwell Hospital.

The 2018 Autoimmune Focus meeting took place in September at the Hilton Metropole Hotel in Birmingham. The meeting was organised by Werfen and provided an opportunity for scientists and clinicians working in the field of clinical immunology to come together to participate in seminars and debate around current topics in autoimmunity.

A changing paradigm in autoimmune diagnosis?

The meeting was chaired by Dr Joanna Sheldon, Immunology Clinical Lead from St Georges Hospital and Dr Gary Norman, Director of Research and Development for Inova Diagnostics. The day started with a presentation from Dr Norman who reviewed the complexity of autoimmune disease diagnosis. Dr Norman discussed how the developing knowledge around specific biomarkers can help detect unrecognised autoimmune disease. New biomarkers can identify early evolving disease and help stratify patients into subgroups with different disease prognosis, different severity, and different response to drugs. There was a particular focus on new biomarkers for systemic sclerosis such as anti-Th/To and anti-BICD2.

The discussion lead on to new developments in multi-analyte testing and how unique multi-analyte testing solutions will allow clinicians to utilise panels of relevant biomarkers to achieve improved clarity on their patient's current and future status. Watch this space!

Anti-DFS 70 antibody testing – one year on

The next two presentations were on the inclusion of anti-DFS70 antibody identification in the ANA testing algorithm. Speakers for this session were Sofie Schouwers from the Department of Laboratory Medicine at GZA Hospital in Antwerp and Lieve Van Hoovels from the Department of Laboratory Medicine at OLV Hospital in Aalst.

The speakers confirmed that the detection and interpretation of anti-DFS70 antibodies by indirect immunofluorescence (IIF) alone can be challenging with the need for solid phase assays, such as chemiluminescence for confirmation.

Following a discussion around the potential clinical significance of anti-DFS70 antibodies for discriminating ANA positives on healthy individuals and patients with autoimmune rheumatic diseases, a Belgian study was described which included four laboratories and explored the benefits of integrating anti-DFS70 testing into routine practice.

Lieve Van Hoovels and Sofie Schouwers – anti DFS70 testing – one year on

The year-long study concluded that the prevalence of anti-DFS70 antibodies (9.4%) justified the inclusion of the anti-DFS70 antibody analysis in the diagnostic ANA algorithm. Although the exclusion of SARD is largely a clinical diagnosis, the identification of anti-DFS70 antibodies provided an explanation for the presence of high titres of ANA found in some patient groups and helped in clinical diagnostic decision-making.

ANA standardisation – NEQAS survey update

Dina Patel from UK NEQAS gave an update on ANA IIF standardisation. Dina discussed the amount of variation that can be seen when looking at the "same" pattern. This variation can be because of substrate, manufacturer and even reader. It was discussed that one way to overcome this variability is to harmonise ANA reporting using the International Consensus on Antinuclear Antibody Patterns (ICAP). UK NEQAS have included the ICAP classification within the ANA element of the nuclear antibodies and related antigens scheme. Dina discussed the possibility that the subjective nature of ANA testing by IIF could disappear with the introduction of more automated reading systems and this could lead to more consistent IIF results.

ANCA testing in the laboratory

The next two talks were on ANCA testing. Firstly, Sarah Beck, Consultant Clinical Scientist, reported a retrospective study

Dr Gary Norman – A changing paradigm in autoimmune diagnosis.

performed at Heartlands Hospital. The trigger for this study was the revised 2017 *International consensus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis*. The 2017 consensus states that there should first of all be a gating strategy for the testing of ANCAS, then MPO and PR3 should be tested using Immunoassays, before confirmation by IIF. Currently, Heartlands screen for ANCAs by IIF, and then if the IIF is positive, the sample goes on for MPO/PR3 by ELISA. They concluded that the 2017 recommendation could be followed and there would be a reduction in false positives but there were cost implications of screening using solid phase assays.

This talk was nicely followed by a presentation by Dr Joanna Sheldon on what we should be doing with ANCA testing. Dr Sheldon reiterated the importance of only performing laboratory tests to aid diagnosis, to monitor the disease and for disease prognosis. The audience were all then thinking how many tests do we actually perform which don't meet these three criteria?

Autoimmune liver disease

The last three sessions of the day were all related to autoimmune liver disease. The first one was by Dr Gary Norman and looked into novel biomarkers for autoimmune liver disease, such as anti-kelch-like 12 (KLHL 12) and anti-hexokinase 1 (HK 1) – providing opportunities to close the seronegative gap.

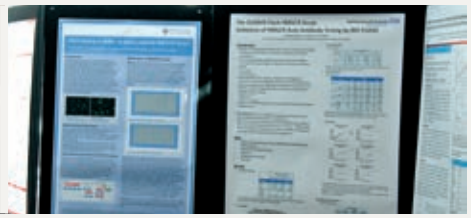
Dr Ye Oo, Consultant Transplant Hepatologist and Clinician Scientist from the University Hospital, Birmingham gave a very clear and informative overview of autoimmune liver disease – specifically around autoimmune hepatitis, PBC and PSC.

The last talk of the day was a very inspiring presentation given by Robert Mitchell-Thain who is Head of Education and Development at the PBC Foundation. He gave the presentation from the view of a patient suffering with PBC. From his own family experiences, he was able to relay to the audience the mental health issues which can occur post-diagnosis. He described the itch of PBC as spiders crawling under the skin, and the tiredness as trying to walk through custard; this put the symptoms into perspective for the audience. He expressed how important self-management is in helping with the long-term condition, as there is currently no cure for PBC.

The 2018 Autoimmune Focus meeting covered a range of current and interesting subjects around autoimmune diagnosis giving an insight into future diagnosis and management of autoimmune disease using important new biomarkers. The meeting also provided a welcome opportunity for discussion and debate around changing thoughts in autoantibody testing.

There were also a number of UK study posters available to view throughout the day.


Discussion opportunities

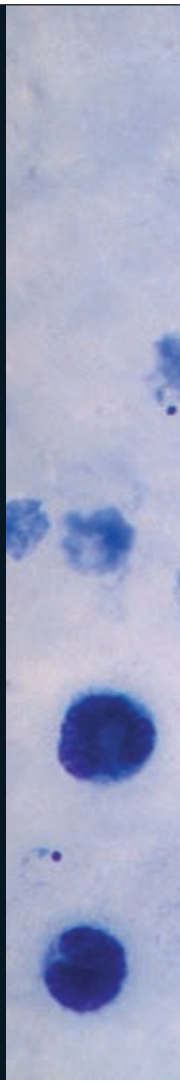

UK study poster viewing

UK poster presentations at the meeting

Poster No	Title	Author(s)
1	Verification of the Automated Inova QUANTA Flash Calprotectin Chemiluminescent Immunoassay	J Bailey & A Sharma Torbay Hospital
2	ANCA Testing in ABMU – Is there a need for ANCA IIF titres?	P Griffiths & Dr T El-Shanaway Morriston Hospital
3	Anti-Phospholipid Antibody Testing in Immunology	P Griffiths & Dr T El-Shanaway Morriston Hospital
4	Performance Comparison of QUANTA Flash Chemiluminescence Immunoassay vs enzyme Linked Immunosorbent Assay – Anti GBM Disease	V Nhalpho, Dr S Pitt & Dr M Tarzi Royal Sussex Hospital
5	Evaluation of Solid-Phase Antiphospholipid Antibody Assays using QUANTA Flash kits on the BIO-FLASH	P Patel, S Tugnait & G W Moore St Thomas' Hospital
6	Processing of QuantiFeron-TB Gold Plus via the QUANTA Link Application	D Hannah Werfen UK
7	The QUANTA Flash HMGCR Assay: Validation of HMCGR Auto-Antibody Testing on the BIO-FLASH	A Woods et al Churchill Hospital
8	A one year retrospective audit on Calprotectin: how well is primary care adhering to the pathway for inflammatory bowel disease?	B Palmer et al Stockport NHS Foundation

QUALITY THICK FILMS FOR MALARIA DIAGNOSIS

Senior Biomedical Scientist **Emma Victory** gives practical guidance on how best to make a thick blood film.



In an increasingly molecular world, microscopy still plays a vital role in malaria diagnosis. Other available methods include rapid antigen tests, quantitative buffy coat, numerous DNA-based assays, as well as clinical diagnosis. But microscopy provides information the other methods cannot. For example, microscopy is the only method which can demonstrate clearance of viable parasites from the blood. Both antigen and DNA-based methods will remain positive for some days (and in some cases weeks) after successful treatment.

In the Public Health England Malaria Reference Laboratory (MRL) we examine thin and thick blood films (where possible) on every patient referred to the lab. Thin films enable species identification of malaria parasites based on morphology of the parasite and changes to the parasitised red blood cells. The parasitaemia (percentage of parasitised RBC) of a patient is estimated using a thin film. This value, which gives an indication of severity of infection, is used to monitor treatment and recovery. Thick films are a concentration technique. In contrast to thin films, a greater volume of blood is used and the entire smear can be examined.

In the hands of an experienced microscopist, thick films are 20 to 30 times more sensitive than thin films for detection of malaria parasites. Relatively speaking, a large volume of blood can be rapidly examined and this is why in some clinical settings thick films are used for screening patients.

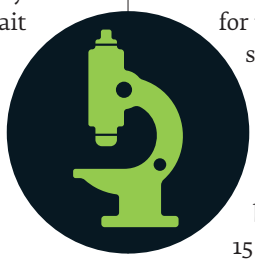
Making thick films

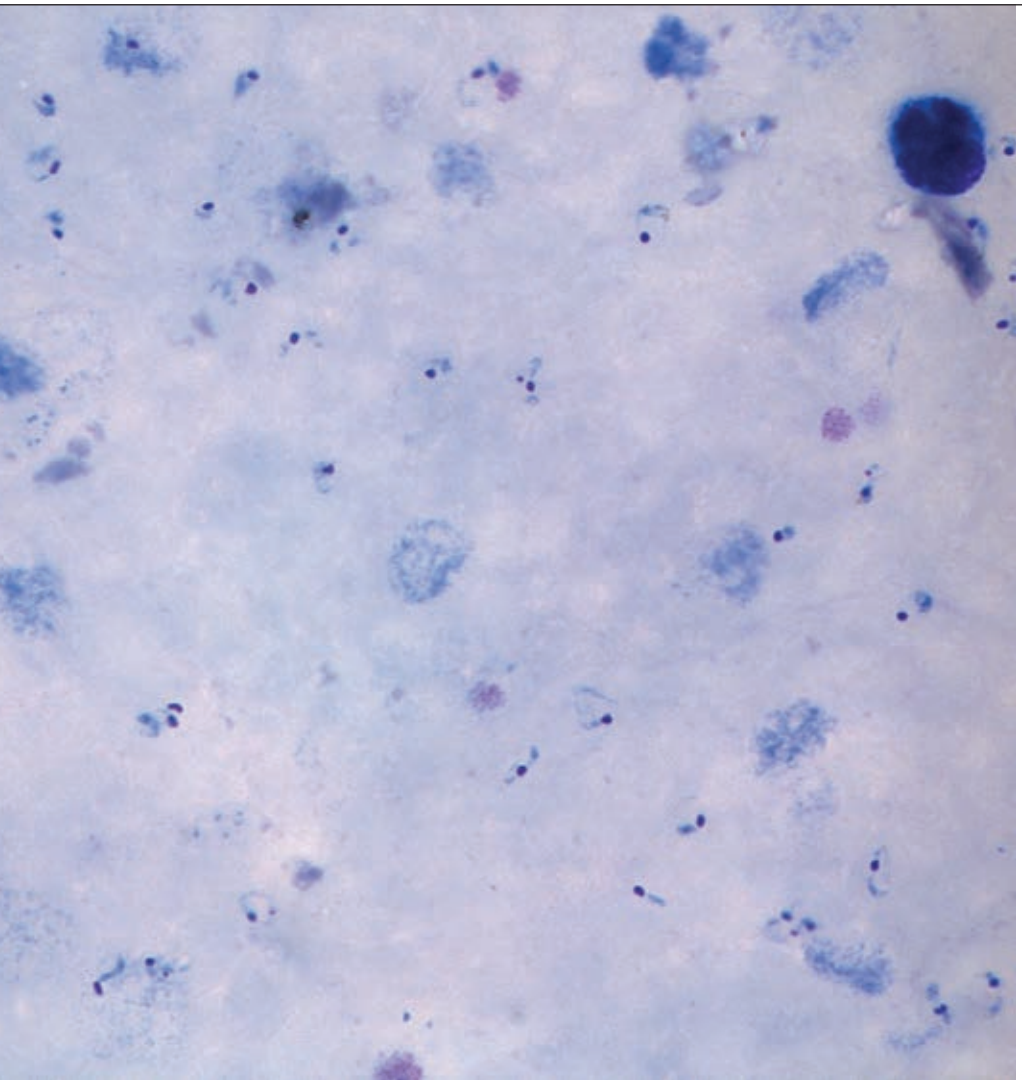
We receive many unsuitable thick films at the MRL, possibly because senders are not routinely examining them in their labs or lack experience in doing so. When films are poorly made we may be unable to examine them. If there is a low parasitaemia there may be no detectable parasites on the thin blood film. This may lead to an inconclusive result. Rapid antigen tests are highly sensitive for *P. falciparum* but they cannot differentiate the non-falciparum species and the sensitivity is much lower for these species. We have molecular assays available in the MRL but they are still not as fast for obtaining a result as a good quality set of blood films in the hands of an experienced microscopist.

Blood films can be made from either a finger prick or from venous blood. They should be made as soon as possible, ideally within two hours of taking blood. Parasite morphology is affected by anticoagulant; the longer the wait between taking blood and making films, the more challenging species identification becomes.

It's unnecessary to measure the volume of blood used to make thick films (but in practise approximately 5 µl is sufficient). Two or three drops should be placed on the slide and the corner of a slide or an orange stick used to join the drops and spread them into an even layer. It is preferable to make films in the centre of the slide. If too close to the edge, they may be rubbed off in transport, or when placed in a rack to dry.

The shape of the smear is not important – they may be circular or ovoid, or even rectangular. The size should be 1-2cm in diameter. Films should be allowed to dry horizontally on a flat surface to ensure they remain an even thickness. Allow at least 30-60 minutes for thick films to dry before staining or packaging them. Consider the level of humidity in your local environment. In high humidity, thick films will take longer to dry. Films may be dried in a 37 °C incubator for 15 to 60 minutes, although direct





Below. An ideal specimen of two thick and two thin blood films
Left. Thick film with trophozoites

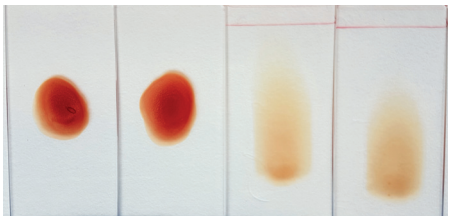
heat should be avoided as this may heat-fix the films. It should be just possible to read newsprint through a thick film when it is dry (prior to staining). If this isn't possible then the film has been made too thick. If too much blood is used, or if the smear is uneven or bumpy, it may not adhere fully to the slide and can flake off before the slide is stained. Or the smear may partly or wholly wash off the slide during the staining process, leaving insufficient material behind to examine.

Different purposes

Thin and thick blood films serve different purposes in malaria diagnosis. Thin films allow visualisation of a monolayer of cells (RBC, WBC, and platelets), along with any intracellular or extracellular parasites. Thin films must be fixed with methanol to preserve all of the details which enable detection and identification of malaria parasites. Thick films are a concentration method. They consist of many layers of RBC stacked on top of each other. Thick films should not be fixed with methanol (or direct heat). During the aqueous staining procedure the unfixed RBC lyse, leaving the remains of WBC and any malaria parasites present behind. If thick films are fixed before staining they will be too dense to examine. When thick films come into contact with methanol vapour unintentionally this can also lead to fixation, e.g. when making thin and thick films if the thins are methanol fixed and then immediately put into a slide box with the thick films this will fix the thicks too, even if only partially, and result in poor or incomplete lysis.

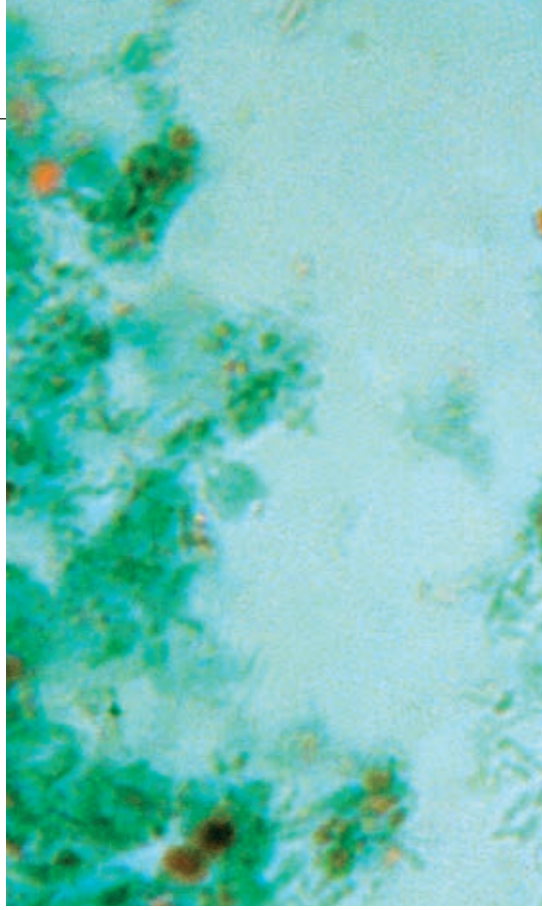
When good quality thick blood films are submitted we have the best opportunity to detect and identify any parasites present in the patient's blood. This enables us to reach a result more rapidly, consequently promoting more effective patient management.

If good quality thick films are made and stained correctly they will be much easier to examine



Thick films are often perceived as too difficult or too time-consuming to bother with, hence they are avoided completely by some laboratories. However, if good quality thick films are made and stained correctly they will be much easier and more pleasant to examine. With a little practice, you might even start to like them as much as thin blood films. BMS

Emma Victory is a Senior Biomedical Scientist at the Public Health England Malaria Reference Laboratory.



HOW TO... USE TRICHROME STAINING FOR ENVIRONMENTAL SURVEILLANCE OF PROTOZOAN HUMAN PARASITES

Can trichrome staining be a cost-effective tool? Parasitology PhD student **Umar Anjum** and colleagues report on a pilot study.

Environmental contamination by protozoan intestinal human parasites has become a significant global threat due to increasing globalisation, climate change and population increase globally.

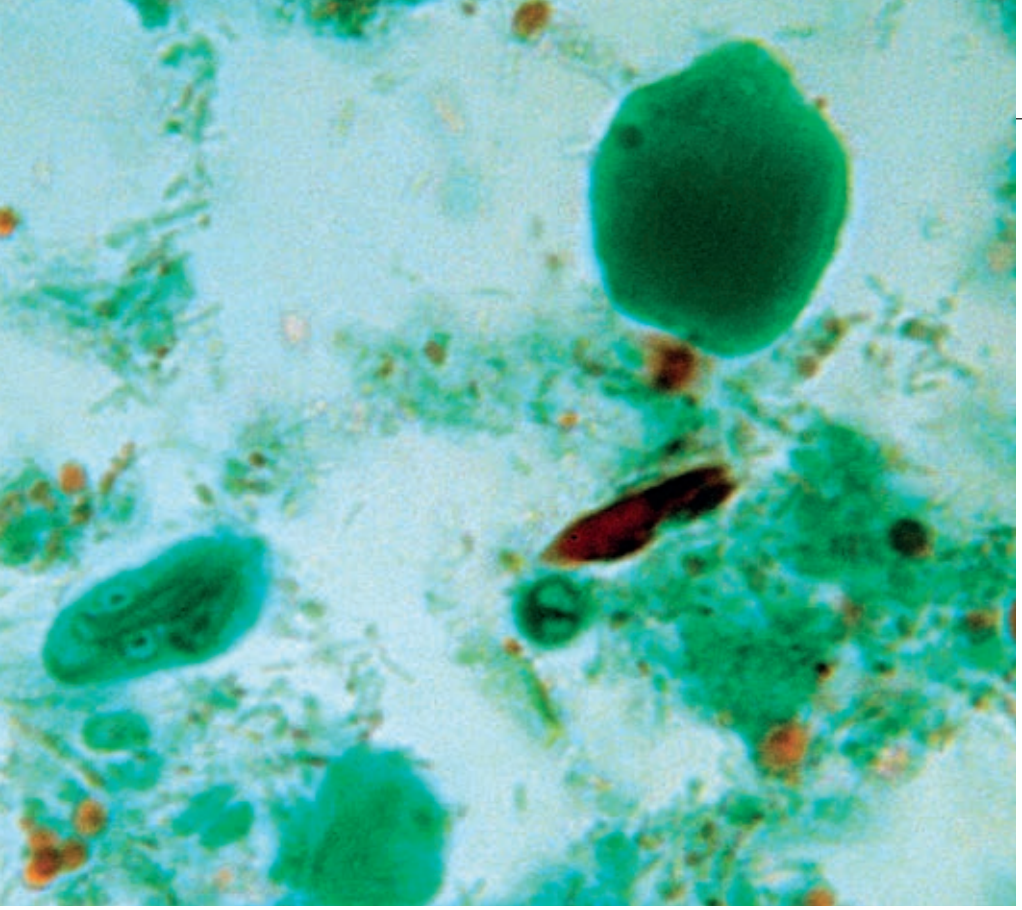
In this communication, we describe a simple laboratory procedure, trichrome staining, as a preliminary step for determining the environmental presence of *Giardia duodenalis*, for which, despite being a worldwide leading diarrhoeagenic human parasite, infection remains underdiagnosed in the UK. To highlight the necessity of the implementation of routine monitoring studies for determining biological contamination in highly populated areas to minimise infections, we describe a pilot study in which we detected the presence of *Giardia* in urban and recreational areas of Leicester. The trichrome staining technique proved to be a sensitive and cost-effective technique for the detection of this parasite in urban areas. The procedure could be easily adopted by relevant authorities with moderate training to perform surveillance studies as a preliminary screening to identify potential risks and perform further thorough studies that are more expensive.

Introduction

Giardia duodenalis (syn. *G. lamblia* and *G. intestinalis*) is an intestinal protozoan capable of infecting a range of different animal species, including humans, which can be found in soil, water and food contaminated with infected animal faeces. Identification of intestinal parasites traditionally depends upon demonstration of their infective forms (e.g. cysts, oocysts, ova or trophozoites) in wet faecal mounts in saline and/or iodine. However, these methods require relatively skilled personnel who can recognise the morphological structures of the infective forms in the very heterogeneous environment found in a stool smear. Normal trichrome stain could be a more sensitive staining technique for detecting *Giardia* and other emerging human protozoan intestinal parasites such as *Entamoeba*.

Trichrome stain

Small portions of the internal part of fresh animal droppings are sampled from urban surfaces, preferably in dry weeks to avoid weather influence. Thin and



Photomicrograph of a *Giardia duodenalis* cyst seen using a trichrome stain

uniform smears are prepared within a biological safety cabinet by using a small amount of homogenised faecal sample. Smears are then fixed in methanol for 10 minutes and air-dried. The staining process consists of immersion of fixed slides in Coplin jars containing 70% v/v ethanol for five minutes and then trichrome stain for 10 minutes. Smears are then immersed in acidified alcohol solution (ethanol 90% v/v and acetic acid 1% v/v) for 5-10 seconds, for colour differentiation. Slides are then immersed twice in 96% v/v ethanol to stop the action of the acidified alcohol solution.

The final step consists of the following dehydration phases: a) 96% v/v ethanol for 5 minutes; b) repeating the same step in a separate 96% v/v ethanol container; c) 3 minutes in 100% ethanol; d) 10 more minutes in xylene and finally e) mounted with DPX to avoid re-hydration. Slides are then ready to be examined under a light microscope.

Environmental pilot study

A total of 21 fresh animal faecal samples were collected from Humberstone Park in Leicester in August 2017. A veterinarian identified the animal species as: seven avian and 14 dog. Smears were stained with trichrome as, described. *Giardia* spp. cysts were observed in three dog faecal samples (21.4%). The cytoplasm of cysts appear dark blue-green being clearly differentiated from other potential artefacts and background.

This pilot study confirmed a preliminary study in which we specifically detected the presence of *G. duodenalis* in one dog faecal sample from 18 animal stool samples collected in Castle Park (central Leicester) in winter 2016, using a highly specific immunoassay technique. Our results would indicate the presence of *Giardia* spp. in Leicester, in which dogs might play a potential role in transmission.

> *Normal trichrome stain could be a sensitive and cost-effective technique for survey studies*

Applicability of trichrome stain

Trichrome stain could be a sensitive and cost-effective technique for the preliminary detection of protozoan parasites in the environment, as compared to conventional wet-mount methods and prior to performing other, more species-specific, techniques. Wet preparations may not be adequate for performing environmental surveillance studies to protect human health, as protozoan parasites could be difficult to detect due to their smaller size and resemblance with artefacts such as food particles, air bubbles and vegetable or fat cells. The chromotrope 2R, a specific component of trichrome stain, has a strong affinity to chromatin, making the protozoan parasites more prominent and easily identifiable.

Conclusions

Trichrome stain could be a sensitive and cost-effective method for the establishment of routine environmental survey studies in highly populated cities for identifying potential hot-spots and risks due to the presence of protozoan human parasites in urban areas, prior to performing more sophisticated species-specific tests.

The staining test could be easily adopted by the relevant authorities with moderate training and/or resources for quick identification of these risks. BMS

Umar Anjum is undertaking a parasitology PhD at De Montfort University. His co-authors are **Fernando Izquierdo**, **Angela Magnet** and **Antonio Peña-Fernández**.

IMAGE: GETTY

MY IBMS NEWS

REGULATION

HCPC SEEKS CHAIR OF COUNCIL

The Health and Care Professions Council (HCPC) is seeking to appoint a new Chair of Council.

The position is open to lay and registrant candidates, and the ideal candidate will have experience of providing strong non-executive leadership and be able to uphold the principles of transparency and accountability in all of the HCPC's activities.

The successful candidate will act as an ambassador for the HCPC, influencing and building effective relationships internally and externally with a range of senior level stakeholders, inspiring confidence in the organisation and promoting the organisation's central commitment to public protection.

The closing date for applications is 9am on Monday 19 November.

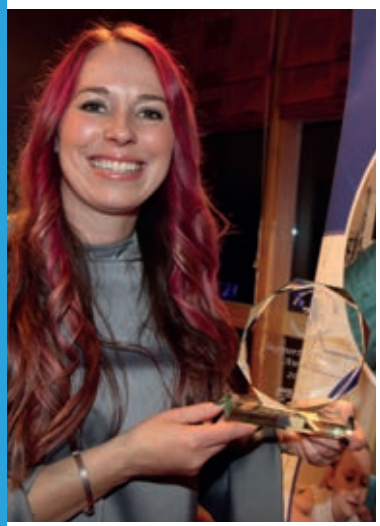
→ For more information and how to apply, visit the HCPC website or contact them on 020 7840 9170.

IBMS LOCAL EVENT

WEST RIDING AGM

The West Riding branch of the IBMS is holding its Annual General Meeting (AGM) on Monday 5 November. The AGM will take place at 6.30pm at the Learning and Library Centre, Old Medical School, at Leeds General Infirmary.

→ For more information, email sarah.lawson12@nhs.net



ACHIEVEMENT AWARDS

Awards for NHS Fife team

The microbiology and emergency care team at NHS Fife has won an award for its improvement to flu testing.

NHS Fife was awarded Top Team at the Achievement Awards 2018, recognising the hard work and dedication of its staff members.

This award is for teams that provide an exceptional service and whose work makes a significant impact on services and patients.

The microbiology and emergency team established an innovative rapid flu testing system at the Victoria Hospital in Kirkcaldy, which reduced the time taken to confirm flu cases from 24 hours to 30 minutes.

The team verified and implemented the new system and trained staff members on its use in only seven days. Results were available in 30 minutes, making it possible for flu and RSV to be diagnosed and treated in real time.

As a result, clinical staff were able to facilitate patient flow through the hospital during a period of intense activity by reducing admissions, discharging earlier and making better use of limited isolation facilities.

Among the winners was IBMS member Lisa Logan, a Senior Biomedical Scientist (pictured). Lisa won the NHS Support Services Award, which recognises excellence and celebrates those with an exceptional work ethic.

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

IFBLS

President-Elect nomination

Alan Wainwright has been nominated as President-Elect of the International Federation of Biomedical Laboratory Science (IFBLS).

It is a not for profit organisation made up of international member associations that represent biomedical laboratory scientists across the world and has direct input into the World Health Organization's development of policy and standards.

Since 2015, Alan, who is the IBMS Executive Head of Education, has been the Institute's representative at IFBLS meetings and has been able to promote the work of the IBMS as an international speaker on education, training and CPD.

Alan said: "Science is a fundamental part of society and culture and, like the IBMS, the IFBLS is uniquely placed to promote our profession. We share a universal language in biomedical laboratory science and we can use our collective knowledge to promote the profession's vital role at the heart of everybody's healthcare.

"With the support of the IBMS I am committed to continuing this work because I see organisational stability, communication and full engagement with all members as crucial to achieving our shared objectives. It is a fantastic opportunity on all levels."

PRESIDENT'S PRIZE WINNERS

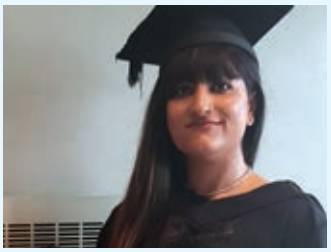
UNIVERSITY OF LINCOLN

Lee-Anne McCarthy received the IBMS President's Prize at the University of Lincoln, following success during her course and the subsequent award of a First Class Honours degree.

During her time at Lincoln, Lee-Anne, pictured with her mother, gained a great deal of knowledge and developed a real passion for biomedical science.

She now intends to pursue an MSc by Research in nanomedicine, with the aim of going on to do a PhD.

ROEHAMPTON UNIVERSITY



Ume Kalsoom was awarded the President's Prize at Roehampton University.

Ume, who is passionate about research in neurodegenerative and neuropsychiatric disorders, said that being a recipient of this prestigious award has given her the confidence to achieve her long-term goals of becoming a successful researcher.

She is currently pursuing an MSc in neuroscience at King's College London and intends to PhD next year.

WISE FELLOWSHIP

Member nets CSO award

IBMS member Siobhan Taylor has been selected for the prestigious Chief Scientific Officer's (CSO) Women in Science and Engineering (WISE) Fellowship.

Siobhan is one of three recipients and is the only Clinical Scientist within a large histopathology department at Gloucestershire Hospitals NHS Foundation Trust.

She is passionate about bringing together the disciplines of genetics and histology to maintain a current and relevant service.

Over the next 12 months, the CSO WISE Fellowship will give Siobhan the opportunity to be mentored by senior leaders in healthcare, industry and academia.

It offers both speaking and ambassadorial opportunities through the CSO and WISE networks. Siobhan will also have the chance to join senior leaders at NHS England advisory meetings.

She said: "This is a fantastic opportunity for me to achieve my personal career goals and gain the skills to help integrate molecular diagnostic testing into histology services.

"I also aim to establish better networks across this area, in order to drive the highest quality patient care."

IMAGES: ISTOCK

JOURNAL-BASED LEARNING EXERCISES

IBMS CPD

Each article's contents should be read, researched and understood, and you should then come to a decision on each question. The pass mark is 17 out of 20 questions answered correctly. JBL exercises may be completed at any time until the published deadline date. Please select your choice of correct answers and complete the exercises online at: **www.ibms.org/cpd/jbl**

DEADLINE WEDNESDAY 6 FEBRUARY 2019

	Analysis of the cytomorphological features in atypical urine specimens following the application of The Paris System for Reporting Urinary Cytology. Glass R, Rosen L, Chau K *et al. Acta Cytol* 2018; **62** (1): 54–61. Assessment No: 110818		**BK and JC virus: a review.** Pinto M, Dobson S. *J Infect* 2014; **68** (Suppl 1): S2–8. Assessment No: 110618
01	This study assessed the performance and utilisation of morphological features in the diagnosis of benign urothelial lesions.	01	JC and BK are named for the patients from whose samples the viruses were first isolated.
02	The diagnosis of atypia on urinary cytology has not been a cause for concern to cytopathologists.	02	The polyoma genome is organised into three regions which all contain genes encoding antigens associated with tumours.
03	The authors agree with other studies that clusters of cells in voided urine remain a complicated entity.	03	JC virus has been found to bind with an alpha (2, 3) sialic acid N-linked glycoprotein receptor on host cells.
04	Patients identified for the study were those with atypical urine cytology who underwent a subsequent bladder biopsy.	04	BK virus can be found in faeces, respiratory secretions and blood, but the most common site of latency is renal tubular epithelial cells.
05	Large nucleoli were the feature that had the highest intra-observer reliability.	05	JC and BK virus can be detected in the urine of asymptomatic immunocompetent patients; this is a common finding during pregnancy.
06	299 specimens were identified for the study and Cytospin preparations were subsequently prepared.	06	BK virus infection can be associated with interstitial pneumonitis.
07	In 2014, the Papanicolaou Society of Cytopathology recommended a urine cytology diagnostic scheme.	07	CT and MRI scans of the brain and analysis of CSF can help in the diagnosis of progressive multifocal leukoencephalopathy, but brain biopsy is the gold standard test.
08	Hyperchromasia (72.03%) and irregular nuclear borders (73.73%) were commonly found in malignant specimens.	08	Detection of BK virus in urine by PCR can be difficult to interpret clinically.
09	One study found the presence of benign fragments in voided urine carries a 6.6% risk for LGUN.	09	PCR assays for detection of BK virus in plasma are reported to have a positive predictive value of 100%.
10	The study applied The Paris System (TPS) criteria to specimens diagnosed as atypical to compare TPS with the current system of reporting.	10	BK virus-associated nephropathy is associated with reactivation of the virus following renal transplant.
11	The presence of tissue fragments in voided urine can carry a risk for urothelial malignancy.	11	BK viruria is seen in 5–10% of patients post renal transplant.
12	The Paris System for Reporting Urinary Cytology was published in 2016.	12	Haemorrhagic cystitis associated with BK virus occurs in bone marrow transplant patients and incidence is reported to be increased when the patient experiences graft-versus-host disease.
13	Due to the low level of interrater reliability, only 118 of the original 299 cases were analysed.	13	Activity of the JC virus large T antigen has been implicated in colorectal cancers.
14	One study found that pathologists not involved in the creation of TPS had lower rates of AUC reporting.	14	The site of latency for JC virus varies, but includes tonsils, bone marrow and brain.
15	ThinPrep cytology is known to reduce the appearance of papillary tissue fragments.	15	Primary infection with BK and JC viruses is not common in childhood, and patients under 15 years usually experience severe respiratory symptoms.
16	The study authors found that high N/C ratio lacked specificity when seen in groups of cells and was not associated with malignancy.	16	BK virus disease post-transplant is not due to reactivation of latent virus while the patient is on immunosuppressive therapy.
17	Coarse chromatin is more specific than other individual features in the diagnosis of urinary cytology.	17	Progressive multifocal leukoencephalopathy occurs in around 80% of patients with AIDS.
18	The use of TPS criteria did not allow the group to identify higher-risk patients in their study cases.	18	Human polyoma viruses have been found to share less than 60% homology with SV40.
19	An increased nuclear-cytoplasmic ratio was not a prediction of malignancy if seen in single cells.	19	Monitoring of plasma BK viral load can be useful in assessment of a patient with haemorrhagic cystitis.
20	The sensitivity and specificity of TPS when applied to atypical cells reported in the study was 68.5 and 58.1%.	20	Treatment for BK and JC virus is aimed at reducing the patient's immunosuppression rather than specific anti-polyoma virus therapy.

REFLECTIVE LEARNING

01	Read the article by Zheng *et al.* (The Paris System for urine cytology in upper tract urothelial specimens: a comparative analysis with biopsy and surgical resection. *Cytopathology* 2018; **29** [2]: 184–8). Compare their findings with those of the Glass *et al.* JLB paper.	01	Critically evaluate the possible links between polyoma virus infection and cancers.
02	If your department has not introduced TPS for urinary cytology, discuss the pros and cons of introducing the reporting system; alternatively, if your department is utilising TPS discuss how this affected the quality of the reports.	02	Discuss the value of detection and typing of polyoma viruses as a means of identification of unknown persons in forensic cases.

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
November		
5 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Birmingham I ecarruthers@bsac.org.uk
5-9 Nov	**National Pathology Week (Stall RHH & NGH)**	Sheffield I scarlet.mccormick@sth.nhs.uk
6 Nov	**Advancing management skills workshop**	Croydon I sue.alexander@rmh.nhs.uk
6 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Salisbury I ecarruthers@bsac.org.uk
7 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Dublin I ecarruthers@bsac.org.uk
7 Nov	**Update in cervical cytology for pathologists, consultant BMS and holders of the Advanced Specialist Diploma in Cervical Cytology**	Bristol I SWRCTC@nbt.nhs.uk
7 Nov	**Waters UK and Ireland clinical user meeting**	London I helen_macdougall@waters.com
7-8 Nov	**Essentials in microscopy**	Southend on Sea I debby.dawson@olympus.co.uk
7-8 Nov	**Update in Cervical Cytology – Scottish Cytology Training School**	Glasgow I scts@nhslothian.scot.nhs.uk
8 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	London I ecarruthers@bsac.org.uk
12-16 Nov	**Biosafety practitioner Level 1 (ISTR accredited)**	Porton Down I nadp.training@phe.gov.uk
13-14 Nov	**Advanced immunohistochemistry**	Sheffield I l.baxter@sheffield.ac.uk
13 Nov	**Manchester bacteriology discussion group**	Manchester I l.coulthwaite@mmu.ac.uk
14 Nov	**FNA cytology**	Bristol I SWRCTC@nbt.nhs.uk
14 Nov	**Medical laboratory assistant – introductory course**	Harrow I LNWH-tr.lrctcbooking@nhs.net
15 Nov	**Mass spectrometry in the clinical laboratory**	Liverpool I john.dutton@uea.ac.uk
15-16 Nov	**SQMDG 2018 Autumn Conference**	Glasgow I m.maclennan@nhs.net
19 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	London I ecarruthers@bsac.org.uk
21-23 Nov	**BM/cytoscreener update course in gynaecological cytology**	Harrow I LNWH-tr.lrctcbooking@nhs.net
22 Nov	**UK NEQAS Reproductive Science Semen Analysis one-day workshop**	Manchester I repscience@ukneqas.org.uk
23 Nov	**Educational workshops 2018: the ongoing challenges of MRSA**	Edinburgh I ecarruthers@bsac.org.uk
23 Nov	**Update course in gynaecological cytology – MDT cases and squamous lesions**	Birmingham I amanda.lugg@bwnft.nhs.uk
27-28 Nov	**Weqas Annual Conference**	Cardiff I contact@weqas.com
27-28 Nov	**Clinical aspects of protein assays**	London I 07384316894
29 Nov	**UK NEQAS cellular pathology-technique non-gynae cytology beginners/refresher workshop**	Gateshead I chantell.hodgson@nhs.net

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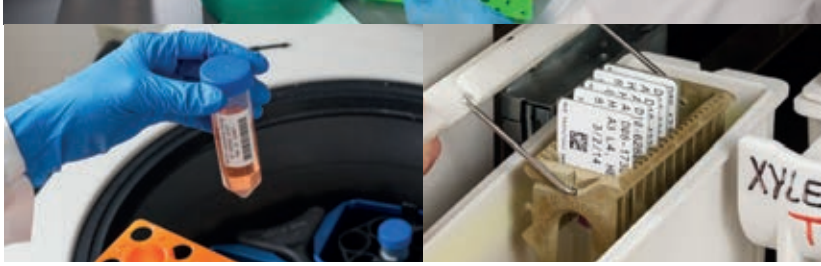

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  - Continuous labels from 12.5 mm up to 3 m long
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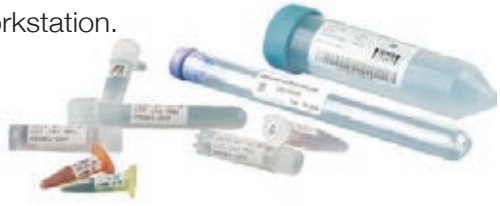
- Use with Workstation.



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MY LAB

HOW CAN YOU HELP US?

This month's article is a little bit different. Instead of writing about helping you, **Jocelyn Pryce**, IBMS Deputy Executive Head of Education, would like to invite you to help her team.

The Education Team receives a large number of grumbles about the time it takes to allocate a verifier or examiner. The delay is not, for the most part, due to delays in the internal office processes but instead is caused by us waiting for examiners and verifiers volunteering to undertake the assessments and this part of the process is out of our control.

Despite recruiting large numbers of new verifiers and examiners through recent training days, we are still struggling to find volunteers to undertake verifications, even in areas where there should be a high number, such as around London.

We have been working hard to streamline our internal processes, and our turnaround times for internal parts of the process are, in most cases, less than a week. But the length of time it is taking for verifiers and examiners to volunteer is increasing the overall total turnaround times.

We are often contacted by trainers or candidates, sometimes rather aggressively "blaming" us for the protracted timeframes in organising their assessments but, as we point out, we are entirely reliant on volunteers. We are very aware of the time constraints within laboratories these days and we are indebted to those of you who offer your services to undertake the various assessments. I would ask that active verifiers or examiners encourage their colleagues to express their interest and volunteer if they are in a position to do so.

I am often asked how many assessments we expect verifiers and examiners to undertake each year and the answer is simple – there's no expectation, although we do suggest at least two a year to maintain currency.

In some areas, where the training ethos is strong, there have been dialogues with managers around a *quid pro quo* relationship where managers release staff to undertake assessments equivalent to the number of live portfolios that will require assessing in their laboratory. This has been a successful tactic in areas where there is a good relationship between laboratories.

We have also been told that the expenses policy can be a barrier to volunteering so, as a response to this, we will include an area within the verification and examination emails where you can easily identify the assessment that you are volunteering for and also add a rough estimation of your expected expenses. This should reduce the protracted email conversation where the team follows up potential costs and seeks agreement for any expenses outside of the policy. In many cases, where a need is identified, expenses above the upper limit can be agreed on a case-by-case basis and an initial estimation can guide early checks for this.

Please also contact us or encourage colleagues to, if you feel that the expenses may be an issue and a barrier to stepping up. We would rather know that you are interested and enter into a dialogue about how we could manage the expenses than for you to feel that we would not sanction your expenses or take advantage of your interest.

Thank you in anticipation of your continued support.

Chief Biomedical Scientist - Histopathology and Biomedical Scientist (Haematology) Band 6 / 7

Isle of Man Government

Chief Biomedical Scientist - Histopathology About the role

Applications are invited from highly qualified, experienced and motivated scientists to join the Histopathology team on the Isle of Man.

We have a great opportunity for a dynamic and forward-thinking Biomedical Sciences Manager who would like to develop their career further as the most senior leader for Histology and Cytology services on the Island. The role will shape the strategic direction for the service and will have operational responsibility for managing the Department.

As a member of the Pathology management team you will be responsible to the Pathology Manager, but will also work closely with the Clinical Director and Heads of Service of the other Pathology specialties. Your ability and experience of driving and successfully achieving change will enable you to provide the leadership and strategic direction required to bring together our teams in the delivery of a patient-focused, cost-effective and high-quality service.

You will hold a relevant professional registration and will have successfully managed within an acute NHS setting. You should have the ability to be creative and innovative to generate opportunities for the service, be able to demonstrate a solid understanding of commercial and business principles and have experience of involvement with strategic planning processes.

You will be responsible for providing an efficient and accurate, quality assured diagnostic laboratory service to all users, facilitating staff training and development, ensuring relevant competencies are achieved to meet service requirements and turnaround times.

More details of the duties of the post can be obtained from Stephen Doyle on 01624 650642.

Biomedical Scientist (Haematology) Band 6 / 7 About the role

This is an interesting and varied post based in a district general hospital laboratory setting however we also perform a range of specialist investigations due to our Island location. The department has a close working partnership with the Royal Liverpool University Hospital. The post offers a rewarding, unique and diverse working environment that comes with an Island setting.

Candidates for the Senior Biomedical Scientist Post must be HCPC registered and have a Masters level qualification in Haematology / IBMS Higher Specialist Diploma or equivalent. A leadership and management qualification is desirable but can be undertaken following appointment. The role requires a high level of theoretical and practical knowledge in all aspects Haematology.

We are primarily looking to fill the Senior BMS post although applicants currently working towards an IBMS Higher Specialist Diploma in Haematology or who have an equivalent level of knowledge and would be willing to undertake the IBMS Higher Specialist Diploma in Haematology will also be considered in a band 6 Specialist Biomedical Scientist role.

The department is equipped with Siemens Advia 2120, Werfen ACL TOP, BioRad Variant HPLC and Benson Viscometer technologies. The post holder will take a lead role and be responsible for the day to day running of the Coagulation section. They will also act as scientific and technical lead for the anticoagulant service point of care testing. Rotation through all sections within the Haematology department is expected as well as Blood Transfusion. There is also a 7 day working rota system for weekend working which attracts a pay enhancement.

There is the opportunity for successful candidates to participate in the voluntary multidisciplinary on call rota, following suitable training and assessment, for which extra remuneration will apply.

The Pathology Department is committed to staff development and will fully support your CPD and future progression.

For more information about the post please contact Mike Kinnish, Chief Biomedical Scientist Haematology on 01624 650629.

Interview expenses and a relocation package of up to £7,000.00 based on receipts is available for this role. For any further information on the relocation package please contact helpmeapply@gov.im. To find out more about the lifestyle, culture and living/working on the on the Isle of Man please visit **www.locate.im**.

This role also qualifies for a recruitment incentive of £3,000 which will be payable in the 1st, 13th, and 25th months of employment.

Subsidised accommodation and assistance with housing costs may also be available.

For more information and to apply today, please visit www.gov.im/jobs and search 7901, for the Chief Biomedical Scientist and search 7545, for the Biomedical Scientist

The closing date for applications is Friday 16th November 2018.

MY LAB

CERVICAL SCREENING DEPARTMENT

Cytology Manager **Kay Ellis** gives a guided tour of her department at Royal Hallamshire Hospital Sheffield Teaching Hospitals NHS Foundation Trust.

Sheffield Teaching Hospitals NHS Foundation Trust cares for 2 million patients each year, and provides diagnostic services from its state-of-the-art laboratories at both the Royal Hallamshire and Northern General Hospital. The cutting-edge facilities enable the Trust to carry out 25 million diagnostic tests each year, with rapid results, and house some of the most advanced diagnostic equipment in Europe.

The Cervical Screening Department is based at the Royal Hallamshire Hospital and provides Human Papillomavirus (HPV) testing and cervical cytology for South Yorkshire and Bassetlaw, the Princess Alexandra Hospital (Harlow) and the States of Jersey. This equates to approximately 110,000 cervical samples a year. To process and report this workload we have 32 staff.

We are one of the six sentinel sites in England piloting HPV testing, and we went live with HPV primary screening women in Sheffield in 2013.

The Department has close links with the North of England Pathology and Screening Education Centre which offers training and updates for all cervical screening staff, including sample takers, plus training for diagnostic cytology and histopathology.

As the cervical screening provider lead, I form part of a team that reports abnormal cervical cytology and supports colposcopy multidisciplinary teams. Quality is vital within the NHS Cervical Screening Programme and there are internal and external standards that we have to meet to continue to practice and comply with national key performance indicators. This means we generate a lot of statistics, so we have an IT specialist who we share with histopathology.

The prep room and HPV laboratory are supervised by an advanced biomedical scientist who looks after the team responsible for sorting out all the samples that arrive by post from Jersey and by courier/local transport from elsewhere. The team sort out the samples; labelling them, entering them on to our laboratory information management system and ensuring that they proceed along the correct pathway through the laboratory. The MLAs process the cytology slides and operate the HPV analysers. We have a dedicated laboratory housing all the HPV analysers plus the preanalytics. We were the first laboratory in the world to get the p480 – the preanalytical stage of the Roche Cobas platform. We have recently installed the Cobas 6800 to increase our HPV testing capacity as we have extended screening to Rotherham and Barnsley.

The screening laboratory and clerical support is supervised by an advanced biomedical scientist, who looks after the workflow through the screening process by cytoscreeners and checkers, with final report, if abnormal, issued by the consultants. The generation of reports ensuring that women who need to be directly referred for colposcopy get their appointments, is also managed by the advanced biomedical scientist.

Sheffield Teaching Hospitals NHS Foundation Trust encourages the training and development of its staff. This is demonstrated by three of our staff, who started life in the lab as cytoscreeners and have been supported through degrees and portfolios to become specialist biomedical scientists We have one trainee who we are supporting through her generic portfolio and are looking to develop her skills within molecular biology.

I am proud to work in the cervical screening department at Sheffield and to work with a dedicated team of professionals who ensure that the women we serve are at the heart of the service we provide. BMS

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*Compared to HPV DNA assays.

I KNOW WE ARE SAVING LIVES

THE POWER OF KNOWING

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