IMMUNOLOGY

A NEW DAWN

Steven Rosenberg on developments in the fight against cancer: *p.16*

MICROBIOLOGY

THE NEED FOR SPEED

The potential for rapid molecular methods in clinical microbiology: *p.25*

CLINICAL CHEMISTRY

TUMOUR MARKERS

The development and application of two vital tumour markers: *p.28*

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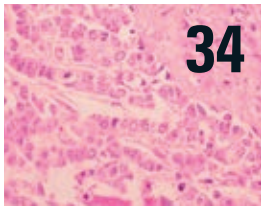

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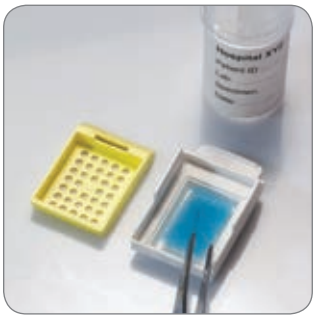

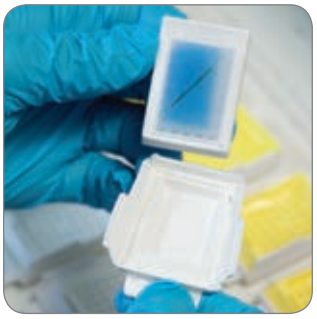

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A.MENARINI diagnostics

STRANGER THAN FICTION

With massive change on the horizon for healthcare, diagnostics has a key role to play in the future.

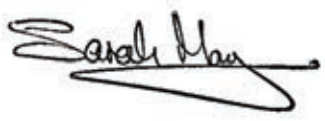
I am currently enjoying a somewhat strange reading diet of 1950s science fiction. It's a pleasant, albeit curious, way of passing the daily commute that doesn't overly challenge the intellect and gives an amusing opportunity to compare some of the futures anticipated by authors of 60 years ago with the realities we now know.

I found the concept of space travel to Mars and Venus by 1997 somewhat naively ambitious, but another author's concept of a eugenics programme to limit the cost of healthcare brought about by an expanding and increasingly ageing population was far more imaginable and hence chilling. Chilling because the book had been written less than 10 years after the birth of the NHS and although it had anticipated the consequences of human expectations and financial sustainability of unlimited healthcare free at the point of delivery, the solution was the product of a corrupt and dystopian society.

An unprecedented and unsustainable demand challenging the current funding envelope is the reality we now face and the primary objective of the varied and multiple modernisation plans is to ensure our healthcare remains free at the point of delivery, without bias or discrimination. Technology and the genomics revolution are going to change healthcare massively over the next 10 years and lead inevitably towards the management and reduction of risk of disease to reduce the need for treatments and cure.

I know that pathology is facing pain and uncertainty as it undergoes reconfigurations and consolidations and I am fearful that the enthusiasm for cuts will damage the very service that will be helping deliver the prevention based medicine of the near future; diagnostics, I am convinced, will be the key to delivering targeted and affordable healthcare. The apparent inefficiencies that are thought to still exist in pathology are nothing compared with the bigger inefficient systems whereby patients are kept in hospital longer than is required because of limited availability of imaging services outside core working hours, the multiple individuals and departments that still seem to operate as isolated episodes in what is supposed to be a continuous care pathway and the lack of social care that delays discharge for many. Our future will be determined by brilliance and innovation and impeded by bureaucracy and administration.

I'd like to finish with an anecdote that has come to mind through my literary foray into imagined futures. I was at a meeting around five years ago where a senior advisor to the health departments stated that "we won't be using microscopes in five years time". OK, so maybe space travel to Venus and Mars by 1997 wasn't such an outrageous projection.



Sarah May
Deputy Chief Executive

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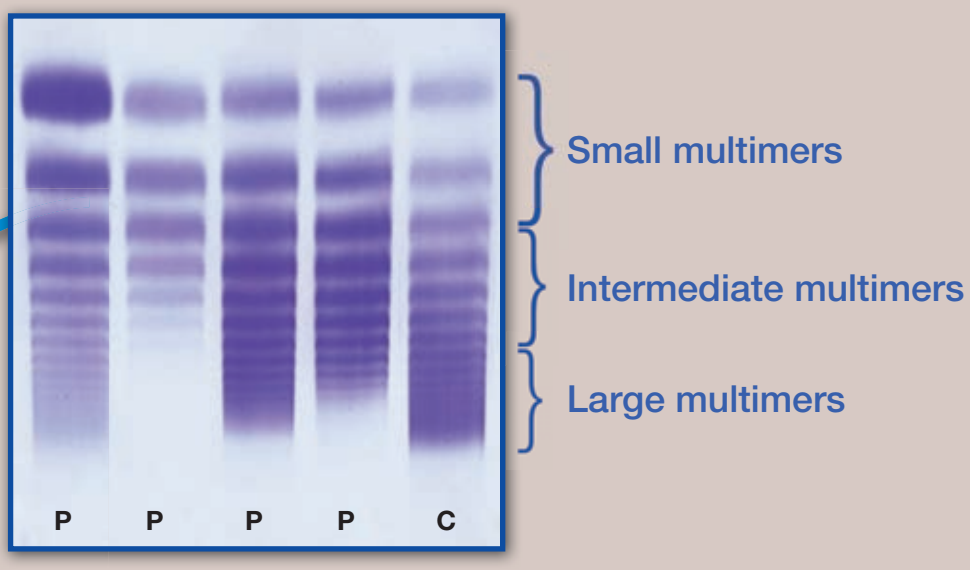

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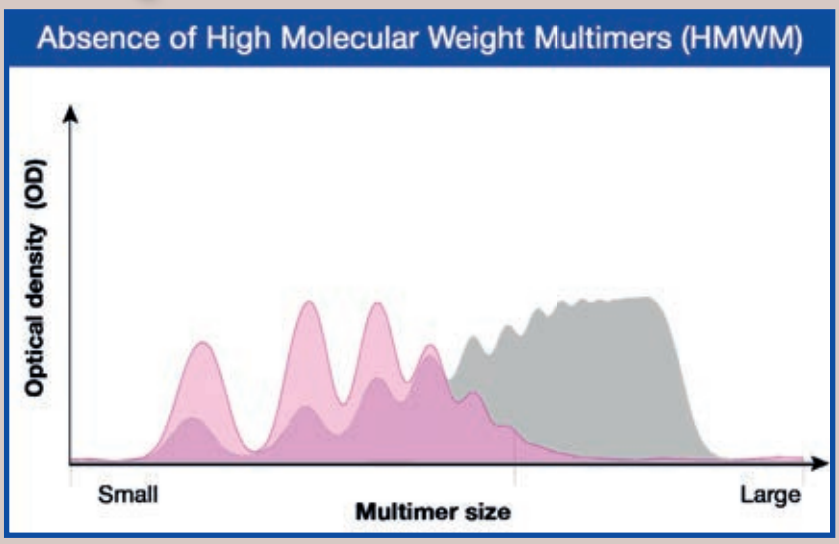

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SCIENCE NEWS IN NUMBERS

ALCOHOL AND ABSENCE

Researchers say teetotallers have up to a 50% higher risk of absence from work for a range of physical and mental ailments.

The Finnish Institute of Occupational Health analysed absence records and survey results from more than **47,000 people in Britain, France and Finland**.

Both **excessive and non-drinkers** were between **20%** and **50%** more likely to take a significant amount of time off work for ailments, including mental disorders, muscles and bone problems and some illnesses.

Women who consumed **between one and 11 units of alcohol a week**, and men who consumed **between one and 34 units**, had the lowest risk of taking at least a week off.

2 MONTHS

In a study of 38 women (25 full-term and 13 preterm deliveries), all at elevated risk of delivering preterm, non-invasive blood tests were able to accurately classify women who delivered preterm up to 2 months in advance of labour.

"SYPHILIS DOUBLES IN A DECADE"

Syphilis is relatively uncommon, making up less than 2% of diagnosed sexually-transmitted infections in England in 2017.

However, there has been a steady rise with the number of diagnosed cases more than doubling in a decade: 7,137 last year, up from 2,874 in 2008.

1,956 NAILS PAINTED

The Indian charity OYE Foundation has broken two Guinness World Records, in a bid to raise awareness about the prevention of breast cancer.

It held the largest female health awareness lesson ever, which a **record-breaking 1,919 girls attended.**

After which **1,956 girls painted their nails pink** for breast cancer awareness.

49 TEA TOWELS

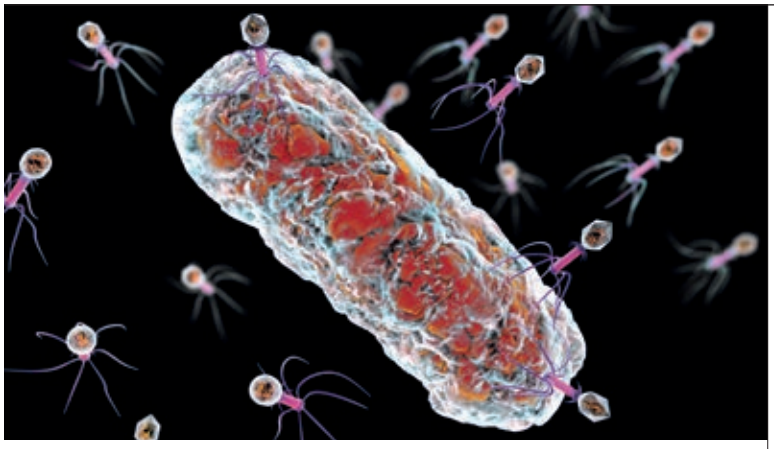
Scientists from the University of Mauritius examined 100 tea towels that had been used for a month and found 49 had bacteria growth.

OF THESE THAT TESTED POSITIVE:

36.7% had coliform bacteria (which includes *E. coli*)

36.7% had *enterococcus spp*

14.3% had *staphylococcus aureus*



SCIENCE NEWS

PRELIMINARY TRIAL

Could bacteriophages replace antibiotics?

A small-scale preliminary trial concludes that bacteriophages could be a viable replacement for antibiotics in the future.

Study results have confirmed the safety and tolerability of using bacteria-specific viruses to eliminate disease-causing bacteria in the gut.

The new treatment could be used in place of antibiotics to rid the gut of harmful bacteria and promote the growth of beneficial bacteria known to enhance gastrointestinal health, immune function and anti-inflammatory processes.

The results from the PHAGE study – the first clinical study in the Western hemisphere to provide patients with bacteriophages – were presented at the American Society for Nutrition annual meeting held in Boston.

The participants tolerated the bacteriophage treatment extremely well, with no adverse events reported during four weeks of treatment.

During the treatment, researchers observed significant decreases in interleukin 4 – an inflammatory marker often associated with allergic response.

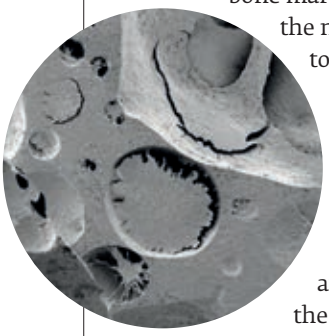
→ **bit.ly/BS_JulyNews01**

BIOMIMETIC ENGINEERING

CREATING HUMAN BONE MARROW TISSUE

Researchers have developed an artificial tissue in which human blood stem cells remain functional for a prolonged period of time.

For years researchers have been trying to reproduce bone marrow in the lab to better understand the mechanisms of blood formation and to develop new therapies.



However, this has proven extremely difficult as in conventional *in vitro* models, blood stem cells lose their ability to multiply and differentiate into different types of blood cells.

Now, researchers have engineered artificial bone marrow niche in which the stem and progenitor cells are able to multiply for a period of several days.

It combines human mesenchymal stromal cells with a porous, bone-like 3-D scaffold and mimics the complex biological properties of natural bone marrow niches.

→ **bit.ly/BS_JulyNews02**

PLASMA PROTEINS

GENETIC ATLAS OF PROTEINS

An international team of researchers led by scientists at the University of Cambridge has created the first detailed genetic map of human proteins.

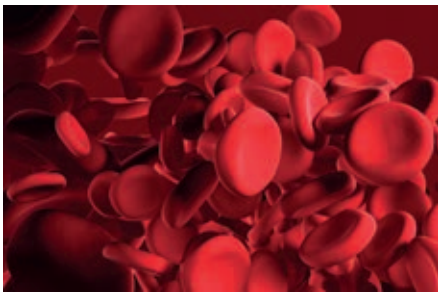
This will be used to enhance our understanding of a wide range of diseases and aid development of new drugs.

The study characterised the genetic underpinnings of the human plasma "proteome" and identifies nearly 2,000 genetic associations with almost 1,500 proteins.

Previously, there was only a small fraction of this knowledge, as researchers could measure only a few proteins simultaneously in a robust manner.

The researchers used a new technology to measure 3,600 proteins in the blood of 3,300 people.

They then analysed the DNA of these individuals to see which regions of their genomes were associated with protein levels, yielding a four-fold increase on previous knowledge.



Adam Butterworth, one of the authors, said: "Compared to genes, proteins have been relatively understudied in human blood, even though they are the 'effectors' of human biology, are disrupted in many diseases, and are the targets of most medicines. Novel technologies now allow us to start addressing this gap in our knowledge."

One of the uses for this genetic map is to identify particular biological pathways that cause disease, exemplified in the paper by pinpointing specific pathways that lead to Crohn's disease and eczema.

The researchers are making all of their results openly available for use.

→ **go.nature.com/2JDzH2i**

IMMUNOTHERAPY

VACCINE TO TREAT LUNG CANCER

A first-of-its-kind treatment vaccine has moved into a phase I clinical trial for patients with non-small cell lung cancer.

AST-VAC2 is a collaboration agreement between Cancer Research UK and Asterias Biotherapeutics Inc.

Cancer Research UK will manage the initial clinical development of AST-VAC2, which is a promising immunotherapy candidate that is derived from a standardised human embryonic stem cell line.

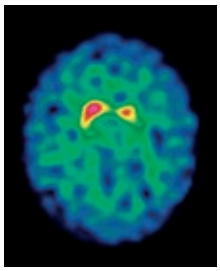
If shown to be safe and effective, it's hoped that AST-VAC2 could be used as an additional treatment for patients who no longer have advanced disease, but whose lung cancer is at high risk of coming back, or in combination with other treatments for patients with advanced disease.

Dr Nigel Blackburn, Cancer Research UK's Director of drug Development, said: "This vaccine trial is a pioneering approach to improving treatment for lung cancer, the biggest cause of cancer death worldwide.

"By coupling our expertise with a leading biotechnology company, we've accelerated the development of this experimental treatment by years."

NEURODEGENERATIVE DISEASES

MOLECULAR MECHANISMS OF PARKINSON'S



Detailed brain cell analysis has helped researchers uncover new mechanisms thought to underlie Parkinson's disease.

For years, scientists have known that Parkinson's is associated with a build-up of alpha-synuclein protein inside brain cells. But how these protein clumps cause neurons to die was a mystery.

Using a combination of cellular and molecular approaches to compare healthy and clumped forms of alpha-synuclein, a team led by scientists at the Francis Crick Institute, found that clumps of alpha-synuclein damaged key proteins on the surface of mitochondria, making them less efficient at producing energy.

They also triggered a channel on the surface of mitochondria to open, leaking out chemicals that tell the cell to die.

→ **go.nature.com/2JZfrl1**

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WHAT'S HOT AND WHAT'S NOT

HOT

FRUIT

A programme has been launched in Michigan in the US in which children are "prescribed" fresh fruit and vegetables, with vouchers that can be redeemed at a farmers' market.

HOT

WRINKLES

US researchers claim our brains are pre-wired to perceive people who have wrinkles around the eyes when smiling or frowning as more sincere.

HOT

ORANGE PEEL

The mechanics of how oranges release fragrant oil when squeezed could be mimicked to develop a less expensive way to deliver airborne medication, say scientists.

NOT

GENE EDITING

Therapeutic use of gene editing with the CRISPR-Cas9 technique may inadvertently increase the risk of cancer, according to a new study from Karolinska Institutet and the University of Helsinki.

NOT

VENDING MACHINES

A study of 5,222 employees across the US found that the foods people purchase at work tend to contain high amounts of sodium and refined grains and little whole grain or fruit.

NOT

DIGITAL RECTAL EXAMINATIONS

Digital rectal examinations for prostate cancer are "unnecessary" and GPs should refer patients regardless of the results, says a new study.

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STEM CELL BIOLOGY

"Mind-boggling" conversion to neurons

Human immune cells in blood can be converted directly into functional neurons in the laboratory in about three weeks, say scientists.

This is possible with the addition of just four proteins, researchers at the Stanford University School of Medicine in the US have found.

The dramatic transformation does not require the cells to first enter pluripotency, but instead occurs through a more direct process called transdifferentiation.

The conversion occurs with relatively high efficiency — generating as many as 50,000 neurons from 1millilitre of blood.

It can be achieved with fresh or previously frozen and stored blood samples, which vastly enhances opportunities for the study of neurological disorders, such as schizophrenia and autism.

Marius Wernig, one of the authors of the study, said: "This technique is a breakthrough that opens up the possibility to learn about complex disease processes by studying large numbers of patients.

"It's kind of shocking how simple it is to convert T cells into functional neurons in just a few days. T cells are very specialised immune cells with a simple round shape, so the rapid transformation is somewhat mind-boggling."

→ **bit.ly/BS_JulyNews03**

HIV RESEARCH

VIRAL SUPPRESSION HELPS TO PREVENT AIDS-DEFINING CANCERS

Early, sustained antiretroviral therapy that results in long-term viral suppression, helps to prevent AIDS-defining cancers and, to a lesser degree, non-AIDS-defining cancers, it is claimed.

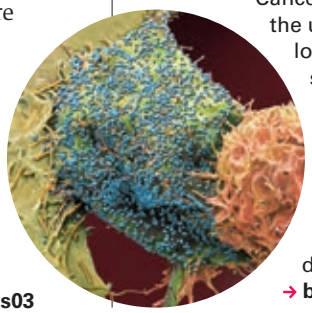
However, patients with long-term viral suppression still had excess cancer risk, compared to uninfected patients.

The study is the first to examine the effects of prolonged periods of viral suppression and potential cancer prevention benefits for the ageing population of persons living with HIV.

Viral suppression is a key component of HIV treatment, and studies have shown an association between prolonged viral suppression and decreased risk for some types of cancer.

However, no studies have specifically focused on the effect of sustained viral suppression on overall cancer risk.

The study compared cancer rates for 42,441 HIV-positive veterans with 104,712 demographically-matched uninfected veterans from 1999-2015.



Cancer risk was highest in the unsuppressed state, lower in early suppression, lower still in long-term suppression, and lowest in uninfected patients for all cancer, AIDS-defining cancer, virus non-AIDS-defining-cancer.

→ **bit.ly/BS_JulyNews04**

UNDER THE MICROSCOPE

This month: The midcingulate cortex

What is the midcingulate cortex?
It is mysterious area of the brain located deep in the cerebral cortex, the function of which has remained elusive to researchers, despite decades of research.

Has this been in the news?
Yes, it has indeed. Researchers claim that they have a "promising new way to understand what the midcingulate cortex (MCC) does". This is significant as dysfunction of this brain area is implicated in a variety of neurocognitive disorders, including Parkinson's disease, ADHD and depression.

What do we already know about it?
Previous research suggests the MCC may help sustain the execution of difficult or mundane tasks. But isolating its exact function is difficult, as it is activated by most events in most tasks.

So what happened with the new research?
A computational model was used to predict the functions of the MCC while people performed a series of daily tasks on a computer, such as making tea or coffee, while their brains were scanned using neuroimaging. The results of an innovative data analysis technique showed that the MCC tracks the progression of a task during its execution, which is encoded as complex patterns of activity across the brain area.

What does that mean?
It suggests that standard approaches for analysing MCC function overlook the major portion of information encoded by this brain area. Rather, they indicate that MCC encodes the distances between representations of task events in task space, revealing how the MCC sustains the execution of extended behaviours.

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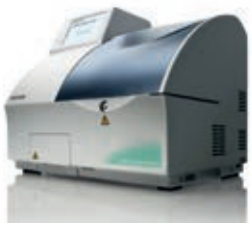

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TECH NEWS

CLINISYS

LIMS SOLUTION

The Integrated Laboratory Services for Barnsley Hospital NHS Foundation Trust and The Rotherham NHS Foundation Trust are now live with their new Laboratory Information Management system (LIMS), CliniSys' WinPath Enterprise solution.

Barnsley and Rotherham Integrated Laboratory Services (BRILS) provides an integrated Pathology service covering all disciplines. Having a modern, robust and safe LIMS was seen as a vital component to achieve their operational.

BRILS has been a CliniSys customer since 2009 and previously used the WinPath version 5 LIMS.

→ **clinisysgroup.com**

LAB INNOVATIONS

LABORATORY INDUSTRY TRADE SHOW

The Lab Innovations trade show returns to the NEC, Birmingham, on 31 October and 1 November 2018.

Free-to-attend and supported by some of the UK's top scientific institutions, Lab Innovations features an exhibition of products and services, as well as learning and business opportunities.

Covering a broad spectrum of industries, including the life sciences, pharmaceuticals, petrochemicals, materials science, food and

drink, visitors can see the latest product innovations and services. There are also seminars and conferences, on a broad range of the latest industry topics.

→ **easyfairs.com/lab-innovations-2018/**

HORIBA MEDICAL UK

DIAGNOSTICS RANGE LAUNCH

Horiba Medical UK has announced a significant development of its *in vitro* diagnostics product offering with the launch of its new Yumizen G range of instruments and reagents.

Marking a milestone in its new product development programme, the Yumizen G range extends Horiba Medical's Haematology portfolio into the complementary field of Haemostasis – a new discipline for the company.

Horiba Medical has developed a reputation for expertise and excellence in blood cell analysis. This has been utilised to deliver the new and comprehensive range of Yumizen G systems and reagents for coagulation diagnostics.

Cleve Wright, Director of Horiba Medical UK, said: "By leveraging our extensive expertise in the Haematology field, we have significantly broadened our scope in blood disease analysis into a complementary discipline."

→ **horiba.com/uk/medical**

THE BIG QUESTION

THIS MONTH WE ASK

"Does healthcare really need a 24/7 pathology service?"

Tony Dedman

Training Coordinator and Method Development Scientist
Homerton University Hospital NHS Foundation Trust

The simple response to this becomes "horses for courses" in that providing a 24/7 service will depend upon the discipline, workload, staffing complement and the degree of clinical cover provided.

Recent NHS Improvement documents suggest that once laboratory collaboration widens, the increase in workloads – in particular from primary care – will inevitably lead to a requirement for working extended hours at the hub laboratories.

It is, therefore, a relatively minor step to move from extended hours to a 24/7 service. However, this would not be true for all disciplines, but just those required to support the critical care areas of the parent organisation.

The ever-expanding repertoire of assays that is available as point-of-care and the options of the "electronic cross match" suggest that spoke sites would not be required to operate a 24/7 on-site pathology service if properly supported by the hub laboratory.

In the current political climate, pathology spending is seen as an essential but expensive service that compromises trust finances. The move to reduce the number of experienced qualified staff will result in a threshold being reached, below which it no longer becomes safe to run a 24/7 service. An unsafe service should equate to no service.

IMAGE: GETTY

Ian Cocking

Pathology Service Manager
Leeds Teaching Hospitals NHS Trust

The short answer is "yes" and to some extent many pathology departments have provided such a service for many years.

In the 20 years I have been a biomedical scientist in microbiology, I have seen considerable change in laboratory service needs, alongside which patient needs and expectations have changed tremendously. They expect to have access to healthcare 24/7 – this includes diagnostic pathology. Can we justify not providing such a service when we ourselves would demand the same when accessing NHS services?

Whilst staff do not always favour late or overnight shifts to provide a 24/7 pathology service, we all feel obliged to provide such a service despite our own personal commitments. Whilst the majority of biochemistry, haematology and blood transfusion departments have well established 24-hour working patterns, microbiology has always been variable in the level of service provided out of hours. But the demands for appropriate antimicrobial stewardship and antimicrobial resistance have seen increasing dependency on rapid and timely testing and reporting of microbiology tests at all times of the day.

We are constantly introducing new rapid diagnostic tests to improve turnaround times to ensure the patient pathway through our services is fit for purpose and effective. Pathology must not be seen as the service that holds up or delays this process. We must all play our part in ensuring NHS services are fit for the patient and fit for the future.

Bamidele Farinre

Specialist Biomedical Scientist
Great Ormond Street Hospital

Emphatically, "yes". It is clear that our dear NHS has entered a new era of change, which has been accelerated by the healthcare reforms, increased burden of rising care costs due to a surge in chronic disease prevalence and the expansion of care for the ageing population. It is inevitable that pathology will move towards 24/7 routine services and providers should commit to meeting patient and public expectations.

Plan to move towards 24/7 service provision must be linked to broader strategic plans

THE NEW DAWN OF IMMUNOTHERAPY

Steven Rosenberg made headlines around the globe for a breakthrough that could make immunotherapy a frontline cancer treatment.

The idea of immunotherapy, or modifying the body's own defence mechanism to fight diseases such as cancer, dates back to the 1890s and the pioneering work of US surgeon William Coley, who established a link between bacterial infections in cancer patients, their immune response to those infections, and the subsequent remission of their cancer. Coley developed a prototype treatment, known as Coley's toxins, but this was soon outpaced by new surgical techniques and the emerging technology of radiotherapy.

The promise of immunotherapy lay dormant for decades, but as biomedical science advanced during the 20th century, it began to reawaken. A key breakthrough came in 1976 with the discovery of how to produce *in vitro* cultures of T lymphocytes – otherwise known as T cells, or the white blood cells that adapt the body's immune response to specific threats.

Miraculous event

Steven Rosenberg, then a young surgeon, now Chief of Surgery at the US National Cancer Institute (NCI) Center for Cancer Research, was involved in the work that built on this discovery. His interest in immunotherapy had started early in his career, when he met a young cancer patient whose tumours has disappeared without treatment. "All aspects of his cancer had gone," says Steven. "He had undergone one of the most rare events in medicine – a spontaneous regression."

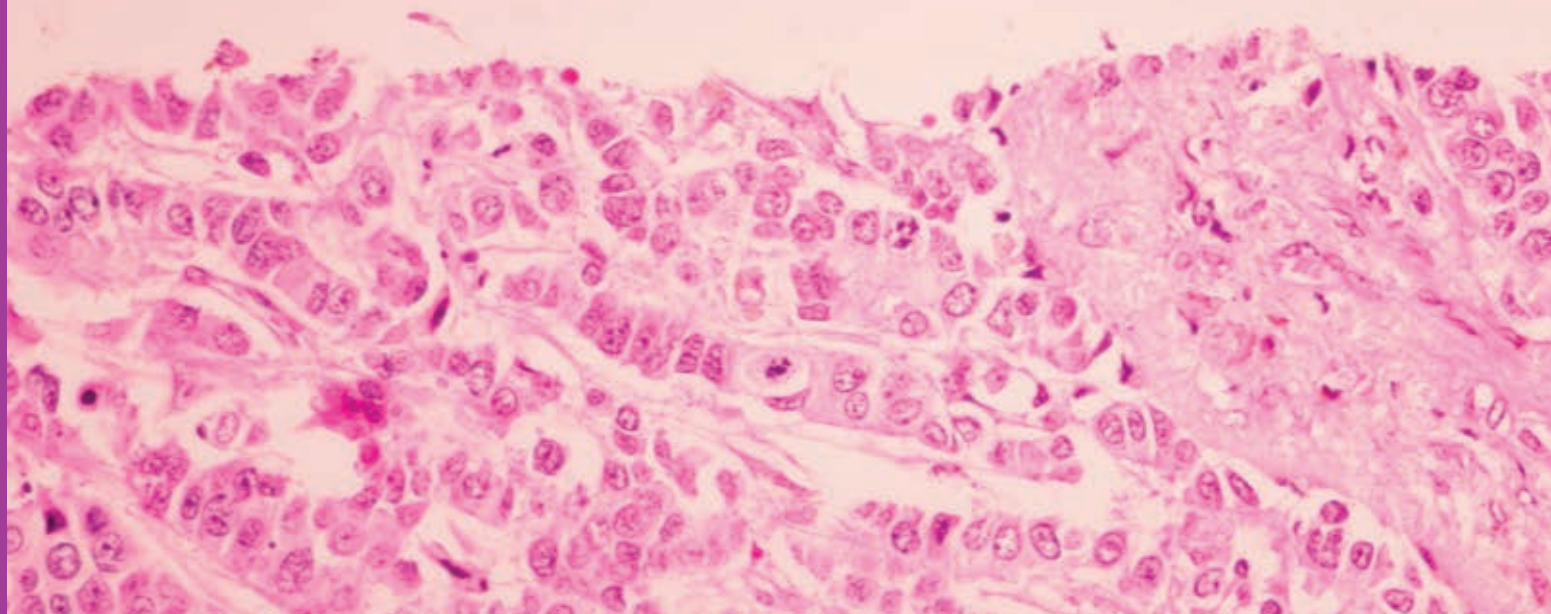
Steven felt the explanation for this had to be buried somewhere in the patient's immune system. "The body has hundreds of billions of lymphocytes," he says, "and somewhere in the body of the patient there had to be lymphocytes that could recognise what was different about the cancer. This led us to identify the cells that were attacking the cancer and then use them to develop a cancer treatment."

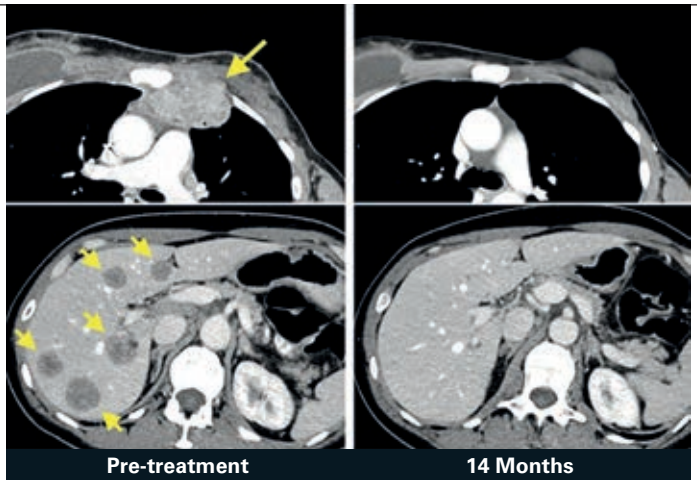
Steven and his colleagues subsequently isolated various types of immune cells and, in a series of early trials, injected them into patients. Initially, success eluded them, but in 1984 they gave their 67th patient a far higher dose of T cells. She responded to the treatment and is still alive today.

Frontline treatment?

The key was to perfect the technique of extracting T cells from a patient's body and growing them by the billions in the lab. This has yielded increasingly positive results, but it's the outcome of their latest clinical trial, published in *Nature Medicine*, that suggests a breakthrough that could see immunotherapy become a frontline treatment for cancer.

Their subject was a patient with metastic breast cancer who had failed to

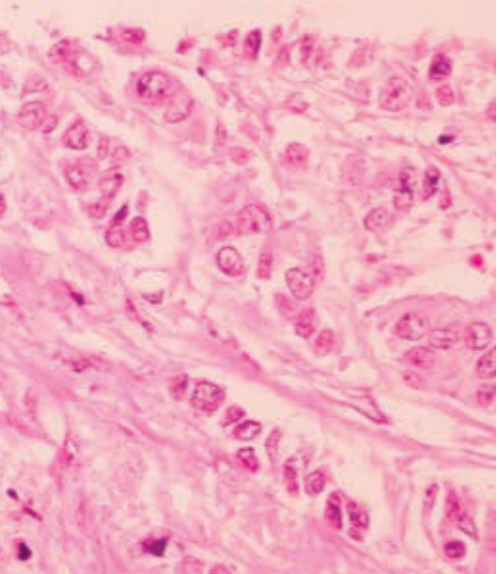




Left. ACT using autologous lymphocytes targeting somatic mutations

STEVEN ROSENBERG

- ✔ Chief of surgery at the National Cancer Institute in Bethesda, Maryland
- ✔ BA and MD degrees at Johns Hopkins University, PhD in Biophysics at Harvard University
- ✔ Residency training in surgery at the Peter Bent Brigham Hospital in Boston, Massachusetts
- ✔ Developed the first effective immunotherapies and gene therapies for patients with advanced cancer
- ✔ Studies of cell transfer immunotherapy have resulted in complete remissions in patients with metastatic melanoma
- ✔ Recent studies have seen regressions of metastatic cancer in patients with sarcomas and lymphomas.



IMAGES: SHUTTERSTOCK/NATIONAL CANCER INSTITUTE

respond to all previous chemotherapy and hormonal treatment.

Steven describes his new technique as "a high-throughput method to identify mutations present in a cancer that are recognised by the immune system. But because this new approach to immunotherapy is dependent on mutations, not on cancer type, it is in a sense a blueprint we can use for the treatment of many types of cancer".

It amounts to a modified form of adoptive cell transfer. This has successfully treated cancers with high levels of mutations, such as melanoma, lung and bladder cancers, but has been less effective with cancers that start in the lining of organs, such as stomach, ovarian, and breast cancers, and have lower levels of mutations.

Targeting tumours

Steven and his team used tumour-infiltrating lymphocytes (TILs) from the patient, which, as their name suggests, specifically target tumour cell mutations.

Their first step was to identify the patient's unique cell mutations by sequencing DNA and RNA from her normal tissue and her tumours. They found 62 different mutations. Next, they tested the TILs to pick out those that recognised one or more of her mutated proteins. The job was then to grow these TILs in sufficient numbers in the lab and inject them back into the patient in order to create a much more powerful immune response against her individual tumours. Her cancer is now in full regression.

"For multiple cancer types that are refractory to all known chemotherapies and immunotherapies, attacking the unique mutations in a patient's cancer can result in dramatic durable regressions," says Steven. "This breast cancer patient is now cancer-free based on all available studies two-and-a-half years after treatment."

Way forward

It's an outcome that he hopes will point the way forward for immunotherapy: "This approach holds the best opportunities for finding effective immunotherapies for patients with the solid cancers. I have showed the slides (pictured) at two American Association of Cancer Research meetings, and have shown that about 80% of patients with common epithelial cancers have T lymphocytes reactive against their own cancer, and that of the 197 immunogenic recognised mutations 196 were unique to the patient's cancer and not shared by any other patient."

Steven feels this insight should change the way cancer is treated: "We need a new paradigm for cancer therapy. Highly personalised treatments are likely to be necessary to make progress in treating common cancers. A unique drug for each patient may be needed. Many oncologists think this is not practical. I think a drastic change is needed and I now know of at least three companies that are working to try to develop this commercially."

Almost 130 years after William Coley first suggested the idea of immunotherapy, Steven and his team have shown that its inherent biological complexities can be overcome, and in the process have taken a giant leap towards to a personalised treatment for a personalised disease. BMS

BIOMEDICAL SCIENCE

Biomedical Science Day takes place on July 19 and the IBMS is calling on its members to join this celebration of the profession #AtTheHeartOfHealthcare, and the incredible hard work and dedication of biomedical scientists.

Following the success of last year's inaugural event, Biomedical Science Day 2018 is expected to be bigger and better, shining an even brighter spotlight on contributions and achievements, which all too often go unacknowledged outside the laboratory.

Taking place on July 19, the birthdate of IBMS founder Albert Norman, it takes the theme "at the heart of healthcare", focusing on the role biomedical scientists play in the healthcare journey. From the newborn heel prick blood test, to the monitoring and treatment of diseases and infections, their work behind the laboratory doors is the foundation on which clinicians base their diagnoses and plan treatment.

Laboratories across the UK and beyond will be marking the occasion, by hosting lab tours, putting up promotional displays, reaching out to schools, taking part in competitions and organising family fun days.

Get involved

And the IBMS is making it as easy as possible to get involved. Ideas and information can be found at **biomedicalscienceday.com**, including

DAY

templates for press releases and invitations, and members can order free promotional materials.

The IBMS is also supporting Harvey's Gang this year. To celebrate NHS 70 they are aiming for at least 70 hospitals to take part in the initiative, so check the website for more information on how to connect with this charity which helps hospital labs provide tours for poorly children.

Following the success of last year's lab selfie photo competition, which brought in more than 300 submissions, the IBMS is also organising more fun competitions this year.

It is looking for the best Biomedical Science Day themed cakes, biscuits, or other baked creations in the biomedical bake-off competition, and photos demonstrating how members are "at the heart of healthcare", with prizes across six different categories. For details of how to enter, visit the IBMS website.

Don't forget to contact the IBMS on the day via social media, using the hashtags #AtTheHeartOfHealthcare or #BiomedicalScienceDay2018 to help promote your events and spread the word about the vital work you do.

Last year, IBMS social media posts were seen by 166,198 people on the day – and this year the aim is to reach many more.

Engage with people

Taking part is well worth the effort, as one of last year's participants attests. Ellen Whiteside is a biomedical scientist based at Blackpool Victoria Hospital, which took part in the first Biomedical Science Day.

Staff organised an information stand in the main hospital entrance, with leaflets to take away and a quiz for children, which attracted huge interest from the general public and hospital staff too.

She says: "We were able to engage with people really well – most people didn't know what we did or that we even existed."

She says their efforts are paying off; helping to generate a "lot more interest in what we do", and that has been built on with further engagement activities through the year.

"It is massively worth doing. Anything that brings us out of the shadows and brings people together can only be positive. It helps people understand what

OPENING THE DOORS OF PERCEPTION

Biomedical Science Day casts light on the profession

BIOMEDICALSCIENCEDAY.COM

JULY 19

we do – especially patients; it is a lot less scary for them when they can understand the processes involved."

Following is a taste of some of the imaginative and impactful events being organised by biomedical scientists across the UK this year.

ROBERT GORDON UNIVERSITY

'LIGHTING THE FLAME OF CURIOSITY'

Rebecca Wright, a Lecturer in the School of Pharmacy and Life Sciences at Robert Gordon University in Aberdeen, says she and her fellow members of the Aberdeen IBMS committee want to "really embrace the day".

They are organising a public engagement event on July 21 at the Aberdeen Science Centre, with support from some of the students at the university and staff at NHS Grampian. Pitching at the nine- to 11-year-old age range, their aim is to open their eyes to the role of the biomedical scientist in healthcare and spark an interest in the subject.

"We felt that, with public engagement for STEM subjects, the earlier the better – we don't think you're ever too young to get involved," says Rebecca. "It's really important that we get the message out there that this is a really interesting and dynamic career pathway."

Stalls representing the clinical disciplines - haematology and blood transfusions, microbiology, pathology, biochemistry, and genetics – will be staffed by HCPC-registered biomedical scientists, who will talk about their work. And children will be invited to try some hands-on activities including a blood typing exercise, and preparing blood smears with bovine blood to look at through a microscope.

"Hopefully they will go away with a bit more of an understanding about the role of the biomedical scientist, or a new fact about the human body, or recognition of biomedical science as a career option," adds Rebecca. "It exposes them at a young age to a really positive experience, which will hopefully light the flame of their curiosity and interest within the subject."

WATFORD GENERAL HOSPITAL

JOINING HARVEY'S GANG

One of the latest laboratories to launch Harvey's Gang tours is at Watford General Hospital.

Ben Sheath, Transfusion Practitioner, Haematology, West Hertfordshire Hospitals NHS Trust, spearheaded the initiative after reading about the charity and its Co-Founder Malcolm Robinson in *The Biomedical Scientist*. The first tour for a five-year-old leukaemia patient went ahead in April, followed by another in June, and a third is planned for this month (July).

"It's something I'd really wanted to do but wasn't sure how to go about it," says Ben. "It's so easy to become so focused on numbers and turn-around times that you lose sight of the fact that there is a patient at the end of it. You can lose that context, which is so important."

The idea came together after he moved roles in December last year, becoming a transfusion practitioner. Stepping out of the lab, seeing patients and working with clinicians, he witnessed the huge gap in understanding between what he'd imagined they were aware of, and what they actually understood about the work of the laboratory.

"It's down to communication – no one gets to see what the other person does," he says. "This is a great opportunity to experience and understand it – not just for the children, but for staff as well."

He says feedback from all sides has been really positive, with parents able to understand the waiting times they face so often, and staff getting a boost from the positive coverage in internal newsletters and the local press.

"The work is something that happens behind closed doors," says Ben. "It's taken for granted, and staff can feel like they are not cared about – so it's good to get that exposure, show the lab off. It really helps bring the team together."

UNIVERSITY OF WESTMINSTER

ILLUMINATING 'THE ROLE WE PLAY IN THEIR HEALTHCARE'

Registered biomedical scientist Carol D'Souza, a Principle Lecturer in Biomedical Sciences at the University of Westminster, is hosting a tour of the university laboratories for a small group of patients and relatives of patients.

The idea grew out of a conversation with two patients, one of whom has sickle cell disease, the other thalassemia, whom she routinely invites to speak about their experience to undergraduate students.

"I've been doing that for the past five or six years and it has always been positively received by the students," she says. "Just last year I was talking to them afterwards and they told me that they didn't know what happened to their samples. By listening in to the lecture they had got to know more about the process, but no one

"It's making them aware of who we are, what we do, and the role we play in their healthcare"

had ever talked them through what happened to a sample."

Carol says that during the visit she will put a blood sample through the haematology analyser, explain the process and the results, and look at blood smears under the microscope to compare normal cells with haematological abnormalities.

Working with biochemistry and microbiology colleagues, the group will also experience biochemistry analytical processes and see what organisms they can grow from hand imprints in agar.

"They have their blood taken and they know about the results – but they don't know how the results are achieved – what happens, who does it and where," adds Carol.

"It's making them aware of who we are, what we do, and the role we play in their healthcare."

VICTORIA HOSPITAL

BREAKING DOWN SILOS

Naideen Forrest, a Specialist Biomedical Scientist based at Victoria Hospital in Fife, is helping to organise an awareness-raising fun day at the hospital entrance, with a host of activities inside and out.

She says: "For a long time, labs have gone unseen and unsung, which can be demoralising. This is a unique opportunity for us to promote what we do and give some insight into what goes on behind the scenes."

The team is organising activities for children including inoculating plates using safe alternatives like jelly and yoghurt, a photo booth, with props to help them look like biomedical scientists, and an augmented reality device, which will allow children to scan and "see inside" each other's bodies.

There will also be posters detailing the work of the labs, information and displays covering topics such as antibiotic resistance, as well as plenty of opportunities to ask questions. Video screens will play virtual laboratory tours, and attendees will be able to book a physical tour on the day as well.

Naideen says the aim is to engage not only children, but crucially to help "the general public and our peers learn about our profession".

She continues: "The NHS is a priceless treasure celebrating its 70th birthday and we are a valuable asset in this service. We want to promote biomedical science and the crucial role we play in a unique and fun way, not just for the general public, but also our peers.

"We will also take the opportunity to break down the silo working within which many professions in the NHS find themselves operating. We hope this is a great success for all participating on the day, and that July 19 2018 will be a day to say 'I was there and I am proud to say I am a biomedical scientist'." BMS

BIOMEDICAL SCIENCE DAY 2017 IN NUMBERS

1

Last year was the first ever Biomedical Science Day

+300

More than 300 people sent in lab selfies

166,198

people saw IBMS social media posts on the day

834

The Institute's dedicated website page attracted 834 visits.

49

The IBMS sent out 49 Albert Norman birthday cards to members born on 19 July.

294

people supported the IBMS Facebook profile ribbon campaign.

Fast molecular diagnostics for tight turnaround times

Turnaround times for diagnostic tests can be an obstacle to effectively controlling healthcare associated infections (HAI), such as methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenemase producing Enterobacteriaceae (CPE), with delayed results leading to ward closures and cancelled operations. Fast molecular diagnostic technology provides a streamlined solution and offers the possibility of decentralised laboratory services to further improve turnaround times. **Julian Bendle**, Manager of the Department of Clinical Microbiology and Infection Control for the Aneurin Bevan University Health Board, describes changes to the department's approach to MRSA and CPE testing.

The Aneurin Bevan University Health Board serves a wide geographical area, covering the counties of Newport, Torfaen, Monmouthshire, Caerphilly, Blaenau Gwent and South Powys. The Board's microbiology services are based at the Royal Gwent Hospital in Newport, with a team of 45 BMSs and 17 MLAs processing around 450,000 samples every year. Bacteriology makes up 80 per cent of the workload and, in January 2015, members of the Trauma and Orthopaedics Department approached the microbiology team to discuss turnaround times (TATs) firstly for MRSA, then for CPE screens.

Under the laboratory's previous culture protocols, MRSA samples required incubation for at least 18 hours before positive colony growth could be confirmed. Consequently, a patient had often been transferred to a ward by the time a positive result was returned, and this unavoidable delay was leading to compromised wards and subsequent cancelled operations. The slow availability of screening results was also impeding the admission of patients requiring urgent operations, and the problem was further exacerbated at weekends, when infection control cover was limited.

Finding a solution

The last few years have seen accelerated development of molecular diagnostics. New PCR-based technologies are transforming the testing process, and enabling fast, on-demand testing using stand-alone instruments. After researching various options and trialling a number of platforms, the department purchased a GeneXpert® system (Cepheid), which offers a TAT of approximately one hour for MRSA testing (Xpert® MRSA NxG). The microbiology services can now provide results within two hours of receiving a sample and, although the underlying technology is very sophisticated, performing the test is straightforward. The system ensures consistently high quality results and allows the department to pick up strains that would be missed using its

Above. The GeneXpert, situated in the Royal Gwent Hospital in Newport

in-house media, as well as enabling better random access testing coverage at weekends.

Expanding the scope

The microbiology team subsequently turned its attention to validating carbapenem resistance testing (Xpert® Carba-R) on the same system, following a CPE outbreak in March 2017 introduced by a patient who had been transferred from another hospital. All the patients on the ward had to be screened and several environmental swabs were submitted, which greatly increased the laboratory workload. This incident highlighted how fast testing could significantly help the infection control team, reducing the department's TAT to two hours and improving the overall service.

News travels

A key aim of any hospital is efficient management of patient flow and reduced waiting times. This fresh approach to testing has placed the department under the spotlight, highlighting how it is working to improve TATs and helping to direct patient care pathways. The resulting improvements in patient management have generated interest in molecular diagnostics from other departments; colleagues across the board can see the many benefits that it brings, and have been surprised by how easy it is to perform the tests using the self-contained platform.

Developing and decentralising testing

The new testing protocol is not simply limited to MRSA and CPE, however, and the microbiology team is currently validating the Xpert® Xpress Flu/RSV assay, with the possibility of introducing additional molecular tests to further improve the service in the future. The availability of these small footprint systems like the GeneXpert is also making decentralised testing a possibility. Plans to build a new hospital – The Grange University Hospital in Cwmbran – will create an ideal opportunity to use an additional system to provide on-site satellite testing. This will be far more convenient than sending samples to the main microbiology laboratory in Newport, enabling quicker TATs. With sufficient training, Band 4 practitioners can easily be brought up to speed on the intuitive system, while a biomedical scientist from the microbiology laboratory can oversee maintenance and quality control.

In summary

The introduction of advanced molecular diagnostics has had widespread benefits for the hospital, improving patient management and flow. Faster TATs for MRSA and CPE testing have undoubtedly prevented compromised wards and cancelled operations, and the GeneXpert platform can accommodate a broad range of tests, including Flu A/B, RSV and CT/NG. The size and ease-of-use of the latest generation of molecular diagnostics platforms also enables decentralised testing across multiple departments and hospital sites, supporting the efficient and effective patient care at the heart of the Aneurin Bevan University Health Board.

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THE NEED FOR SPEED

RAPID METHODS IN CLINICAL MICROBIOLOGY

Microbiologist **Mark Wilks** highlights the potential rapid molecular methods presented in the recent conference of the British Society for Microbial Technology.

Diagnostic microbiology is essentially like gardening, with the leisurely timescale that the word conjures up. Unlike diagnostic virology, where culture has been totally abandoned, rapid molecular methods have made relatively little impact in microbiology.

Many outsiders find this absurd and put it down to the inherent conservatism of the profession, but it's not that simple. If it were, then MALDI-TOF could not have achieved total coverage in large- and medium-sized laboratories in just a few years, although very few laboratories had any experience of mass spectrometry (or any idea of what the term meant).

The difference is that generally cultural methods work in microbiology, but not in virology. Most clinically relevant bacteria can be grown in a reasonable period of time, although you may have to look for the right bacteria in the first place to stand a chance of growing them. Set against this, if the sample was taken when the patient was already on antibiotics, the chances of getting a positive result are greatly reduced, where rapid molecular methods have an apparent advantage.

Uptake of technology

The recent Annual Scientific Conference of the British Society for Microbial Technology focused on the perennial topic of rapid methods and their place in diagnostic microbiology.

Vanya Gant, Clinical Director for Infection at University College Hospital London, gave a thoughtful overview of this area and some of the pitfalls that he has encountered.

The case for rapid diagnostics seems obvious in a patient where severe infection is suspected and treatment cannot wait. Here broad-spectrum has to be used until the results of culture and antibiotic susceptibility results are obtained. In theory, in many cases a switch to a narrow-spectrum antibiotic can be applied and the use of a broad-spectrum antibiotic reserved, thus delaying the development of resistance. There should be improved appropriate treatment and hence outcomes for the patient, improved infection control and outbreak monitoring with rapid identification and typing of bacteria and the detection of possible outbreaks. To the clinician responsible for treatment,

however, much of this seems academic and if the patient is improving on the broad-spectrum antibiotic, why change?

Vanya described his evaluation of a novel micro-array system which gave accurate and rapid speciation of bacteria from positive blood cultures. Although the performance of the system was not in doubt and publication in *The Lancet* provided extensive favourable coverage Vanya asked us if we could guess how many kits were sold. The answer was two.

There are many reasons for this, one of which is that new techniques nearly always cost more than the existing method and can, therefore, have a disastrous effect on the laboratory consumables budget.

Another common problem with molecular methods is distinguishing infection from colonisation – something which is especially true with respiratory and gastrointestinal samples. For example, what is the clinical significance of very low numbers of *Clostridium difficile* or *Clostridium difficile* toxin detected by molecular methods in a patient who is apparently well?

Keep the costs down

Meanwhile, technical developments continue apace – microfluidic chips were described, which may replace quantitative PCR and may turn out to be incredibly cheap. The cost of DNA sequencing is always said to be declining exponentially. In one sense this is true – it is now possible to sequence a human genome in a matter of hours at a cost of about $200. If the human genome is 1000 times bigger than the typical bacterium, such as *Escherichia coli,* it ought to take a couple of minutes and a couple of pence to sequence a bacterium. However, the reality is that it still costs about a hundred pounds to sequence a bacterium and it might take a couple of days or even weeks to batch samples to get the economies of scale and keep the costs down to even that level.

It is possible to reduce the time to diagnosis, but often harder to show it affects patient management

In some cases, manufacturers have become intoxicated with the exuberance of their own technology – DNA sequencers get smaller and smaller to such an extent that some connect to an iPhone and are smaller than the phone itself, but it's hard to see what the value of this could be.

Gemma Clark, a Clinical Scientist from the University of Nottingham, described the introduction of increased efficiency to meet winter demands for rapid detection of respiratory viruses. An in-house system for detecting respiratory viruses by multiplex PCR was replaced by a commercial system provided by AusDiagnostics. The process involved a complete rethink of how the lab was organised, from sample handling and processing, to validation of the new essay to result interpretation.

Turnaround times were maintained or reduced, despite a 30% increase in annual workload, there was improved staff satisfaction and improved EQA performance, which had been a major problem with the existing in-house assay.

Going one step further, Justin O'Grady, Senior Lecturer in Microbiology from the University of East Anglia, gave a talk on rapid meta-genomic diagnosis of hospital-acquired pneumonia. Using the Oxford Nanopore MinION system, he showed it was possible to achieve turnarounds from sample to pathogen genome and antimicrobial resistance results in approximately eight hours.

Whilst it is technically possible to reduce the time to diagnosis by the methods described, it's often harder to show that it actually affects patient management or shows patient benefits. While there are likely to be an increasing number of health economics studies to provide these data, it's a sobering thought that more than 40 years ago Raymond Bartlett, an American microbiologist, showed that unless a report was received on the ward by 11am, when the ward round began, it had no impact on patient management until the next day.

Low tech

In some cases, a low-tech solution may produce impressive results on its own. Consultant Microbiologist at Sherwood Forest NHS Foundation Trust, Mike Weinbren, described a long but successful battle to reduce the time interval between when a blood culture is taken and when the bottle is actually placed on the blood culture analyser. This project did not involve the introduction of complex and expensive new technology but something which was much simpler (at least, in theory) so that the haematology laboratory – which operates for 24 hours a day – could put the blood culture bottles on the analyser immediately on receipt. A comprehensive education programme about the importance of blood cultures and the need for rapid incubation and an extensive audit of the process gave dramatically improved results. BMS

Mark Wilks is Lead Clinical Scientist, Microbiology at Barts Health NHS Trust and a Committee member of the British Society for Microbial Technology.

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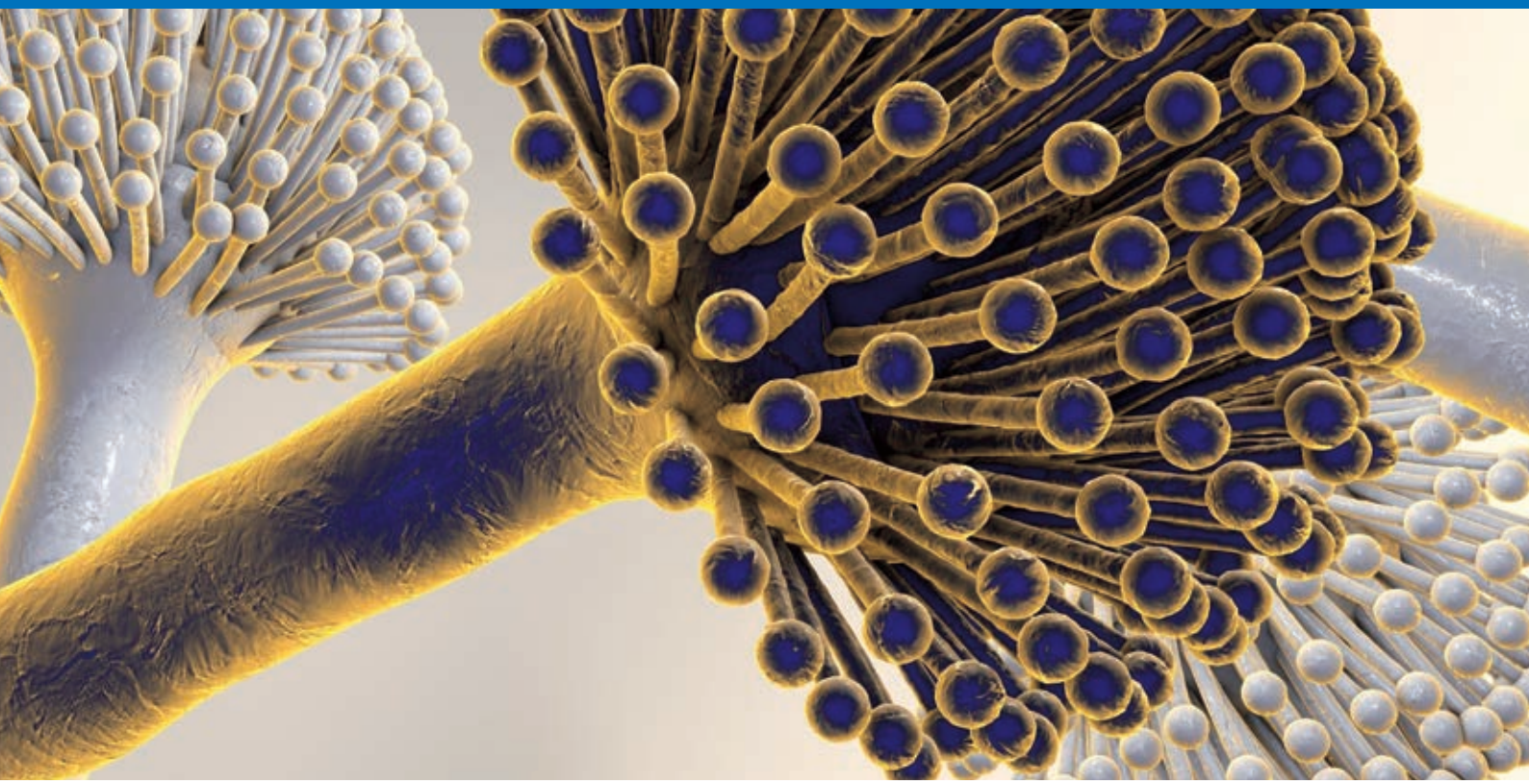

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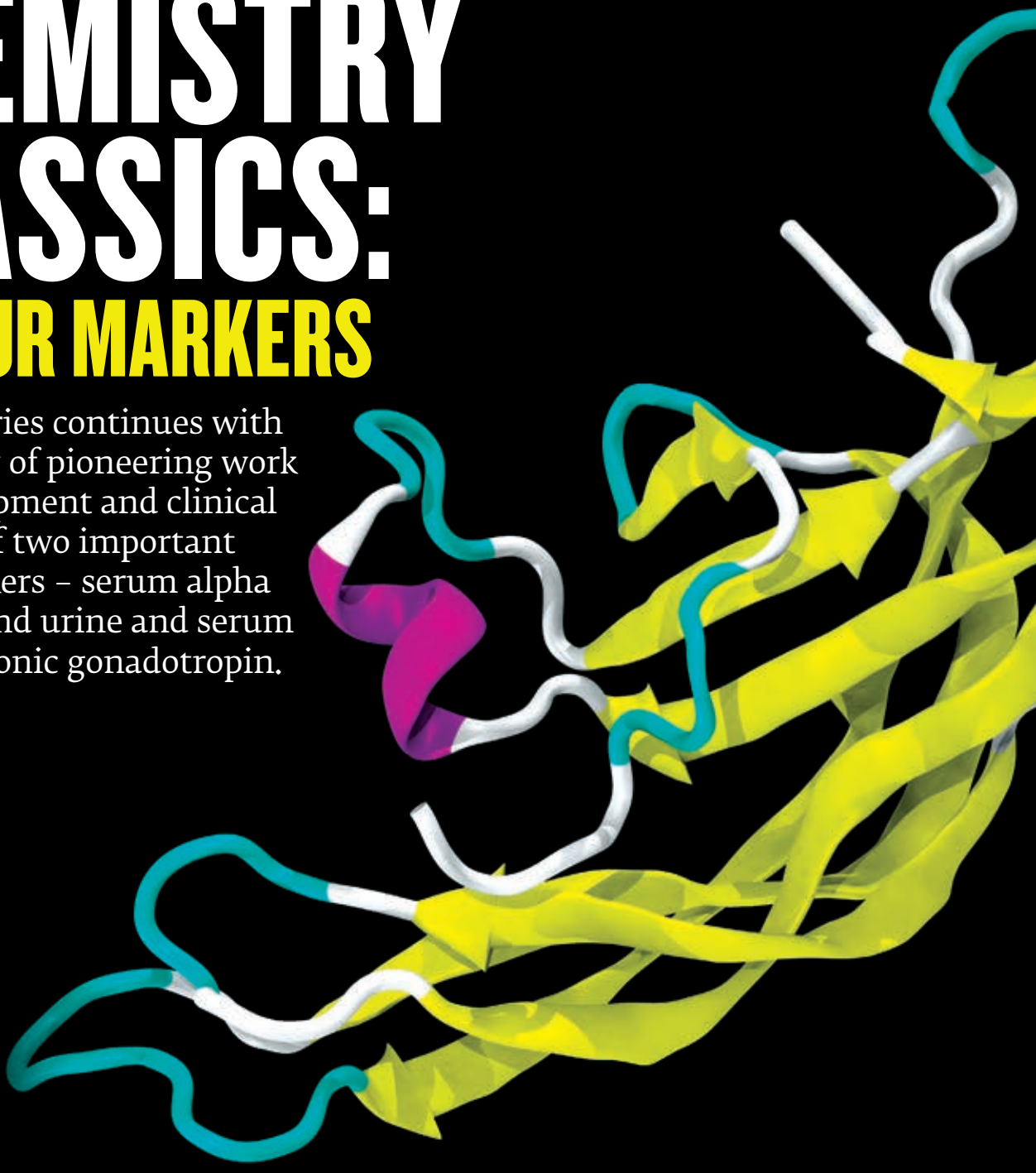
CLINICAL CHEMISTRY CLASSICS:

TUMOUR MARKERS

This short series continues with a brief review of pioneering work in the development and clinical application of two important tumour markers – serum alpha fetoprotein and urine and serum human chorionic gonadotropin.



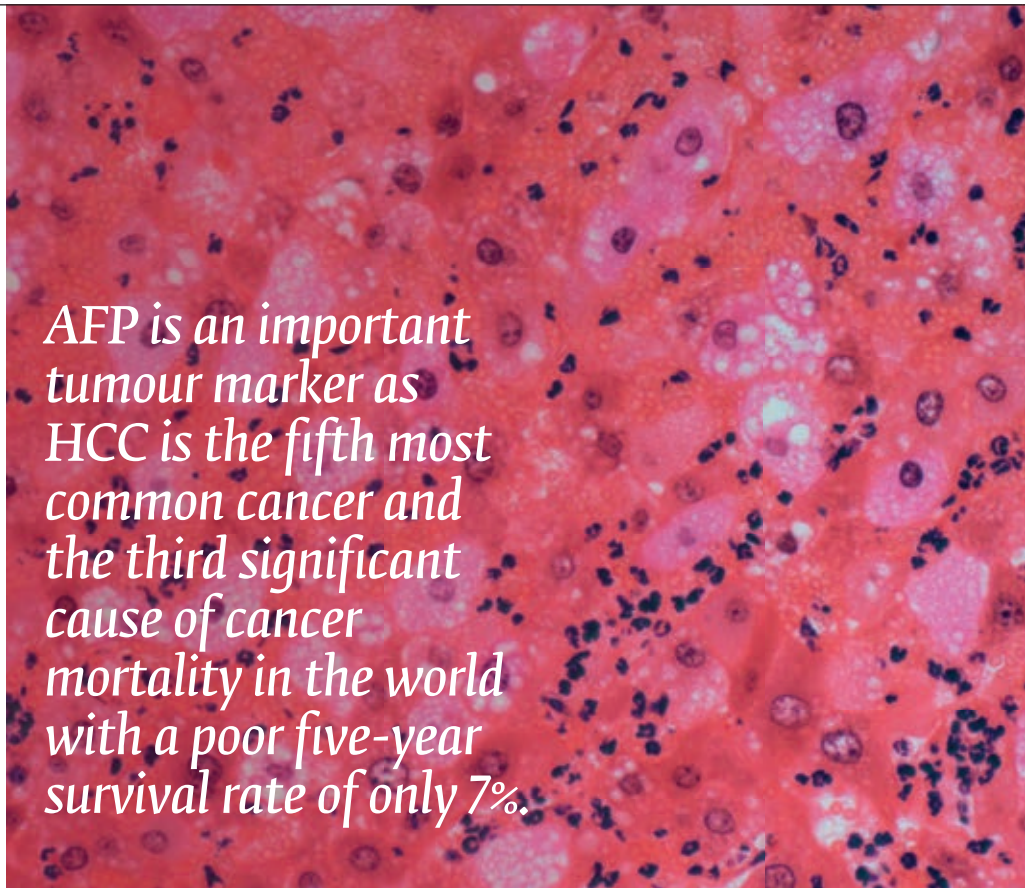
Above. 3D ribbon model of the human chorionic gonadotropin molecule (HCG), based upon protein database entry 1HCN.

Tumour markers (TMs) are substances released by a tumour into blood or urine, or from the host in response to the tumour. Their measurement in serum or urine may be used in screening asymptomatic patients, for diagnosis, prognosis, monitoring treatment and recurrence detection.

Prior to TM development in the 1960s, clinical chemistry laboratories played a limited role in the investigation of cancer patients. Examples of chemical tests in cancers in the early 20th century included urine Bence Jones protein in multiple myeloma, faecal occult blood as a screening test for colorectal cancer and fractional test meals to identify achlorhydria in gastric cancer. Decades later when "routine" manual tests were more developed it was found that serum uric acid, calcium and alkaline phosphatase were of clinical value in leukaemia and bone metastases. Analysis of serum acid phosphatase reported in 1940 showed it was significantly raised in prostate cancer with metastases. Other enzyme assays developed in the 1950s included serum alanine and aspartate transaminases, which were raised in hepatocellular carcinoma.

Tumour markers

Pioneer studies by Ludwik Gross in 1943 and EJ Foley a decade later established the existence of tumour specific transplantation antigens in chemically- or virally-induced animal tumours. Research then proceeded to human tumours and with advances in immunology, combined with intensive studies using novel antibodies and methods, such as double diffusion, gel filtration and immunoelectrophoresis (IEP), a number of tumour associated antigens were identified for more specific tumours during the following 20 years, notably for liver (1964), colon (1965), ovaries (1969) and breast (1971). It was proposed that specific tumour antigens could act as markers for the diagnosis, prognosis and management of certain cancers. In order to formulate TM assays in body fluids, specific tumour tissue extracts were used as immunogens to produce reactive antibodies, with the methods described for qualitative studies. Early quantitative serum methods used immunodiffusion, radioimmunoassay or



ELISA but with advances in antibody linkage technology, more sensitive assays became available and with increased specificity using monoclonal antibodies.

Ideal criteria for tumour markers

The ideal tumour marker assay should have high sensitivity and a low rate of false negatives, high specificity and low rate of false positives, show a positive correlation with tumour volume and extent and the clinical value has been validated by approved prospective trials. The assay should be relatively non-invasive, inexpensive, simple and automated. More than 20 substances have been identified as tumour markers and are in clinical use. However, unfortunately none to date fulfils all these criteria as an ideal tumour marker, and it is surprising that few new TMs have been introduced to clinical practice during the last 30 years. However, the two tumour markers reviewed here have been shown to be clinically useful in diagnosis, treatment and prognosis.

Alpha fetoprotein (AFP)

AFP is a 70kDa glycoprotein, which is homologous to albumin and may perform some of the functions of albumin in the foetal circulation. In 1956, Bergstrand and Czar in Stockholm, identified a new alpha1 globulin in foetal serum using paper electrophoresis. In 1963, Abelev and colleagues in Moscow reported that in chemically-induced and transplantable hepatomas, mice and rats synthesised and secreted AFP into blood. In the following year, Tatarinov reported raised serum AFP in six patients with hepatocellular cancer (HCC). In 1967, Abelev and associates in a landmark article described more fully the clinical importance of AFP in HCC in a larger study using agar precipitation and immunoelectrophoresis (IEP), and reported that serum AFP was also raised in non-seminomatous germ cell (NSGC) tumours of testis or ovary but not in some other testicular tumours. These results have been confirmed in many other studies and serum AFP is now regarded as a first line biochemical test in the diagnosis of HCC, combined with abdomen ultrasound and with serum HCG for NSGC tumours. With a reference range of 0-12ng/ml, a serum AFP greater than 500 ng/ml is regarded as diagnostic of HCC and a failure to clear AFP following surgical liver resection and chemotherapy indicates a poor prognosis. Raised levels may also be found in hepatitis, cirrhosis and biliary tract obstruction and hepatitis B & C are risk factors for the development of HCC.

AFP is an important tumour marker as HCC is the fifth most common cancer and the third significant cause of cancer mortality in the world, with a poor five-year survival rate of only 7%.

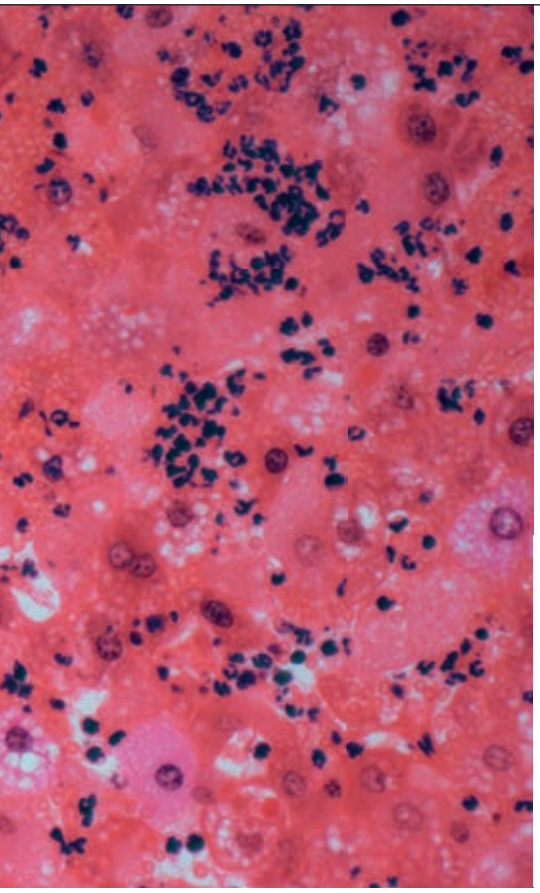
Analytical methods used have ranged from IEP, radioimmunoassay, enzyme immunoassay and immunoradiometric assays during the late 20th century, to the more sensitive types of assay, such a chemiluminescent microparticle inmmunoassay.

The measurement of serum AFP is also highly relevant in screening pregnancies for the detection of open neural tube defects, notably spina bifida with raised results and for Down's syndrome with lower results. The former dates from 1972 with a study that found greatly increased AFP concentration in amniotic fluid and the same Edinburgh group reported an increase in maternal serum AFP the following year. Screening is combined with confirmatory ultrasonography.

Several studies reported in 1984 identified an association between low maternal serum AFP in Downs's syndrome and a group led by Howard Cuckle at St Bart's, London proposed its potential value in screening. This was confirmed in many further studies and maternal serum AFP and HCG are now used worldwide for Down's screening after the first trimester as two of the biochemical markers in the "quadruple" test.

Human chorionic gonadotropin

The isolation of adrenalin and secretin in the early years of the last century and the concept of hormones as chemical messengers, as proposed by the British physiologist Ernest Starling in 1905, encouraged a surge of active endocrine research by many groups, notably in



Germany during the next three decades. This led to an improved understanding of the human ovarian cycle and the hormonal changes that take place in pregnancy. In 1903, Ludwig Fraenkel, professor of gynaecology at the Women's Hospital, Breslau provided experimental proof of the endocrine function of the corpus luteum. With the ready availability of placental tissue, studies by Bernhard Aschner (1912) and Otto Fellner (1913) and Japanese scientist Toyoichi Hirose (1920) showed placental tissue extracts had stimulatory effects on the genital tract, ovulation, and corpus luteum and progesterone production in guinea pigs and rabbits respectively. This clearly demonstrated that the placenta had an endocrine function supporting pregnancy.

Urine HCG as a pregnancy test

In 1928, German endocrinologist Selmar Aschheim and German-born Israeli gynaecologist Bernhard Zondek working at the Berlin Charite, showed that in pregnancy, women produced a high concentration of a gonad-stimulating substance (HCG) in their urine which activated receptors on the gonads of mice. Although the A-Z test took five days, was expensive and required special animal house facilities it had a reported error rate of <2% and was sensitive detecting HCG seven to 10 days after a missed period. A reference station was established in Edinburgh with a postal sample service in 1930 and the procedure was soon used in some London hospitals. In 1931 Maurice Friedman and Maxwell Lapham at the University of Pennsylvania developed a similar technique with large female adult rabbits and the condition of the ovaries was examined after just one day and by 1935 this became the method of choice in London and the United States.

HCG as a tumour marker

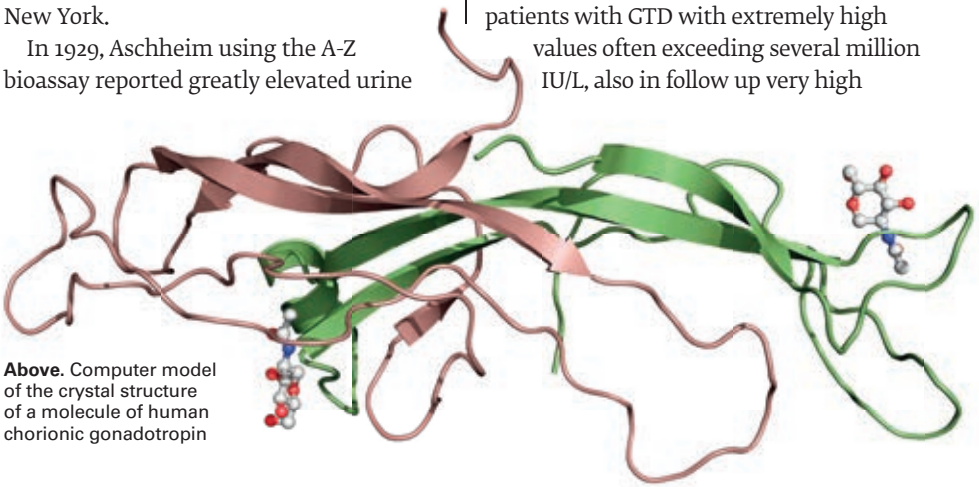
HCG is a 36.7kDa glycoprotein produced by the trophoblast tissue of the placenta in pregnancy and a number of other sites in malignant conditions. HCG stimulates the ovarian corpus luteum to secrete progesterone until the placenta takes over production to sustain pregnancy, it also promotes cell fusion of cytotrophoblast to syncytiotrophoblast and maternal myometrial spiral artery angiogenesis.

HCG is a heterodimer with two glycosylated sub units, the alpha sub unit structure is common to other gonadotropins, for example luteinising hormone, but the beta sub unit of 145 amino acids is unique to HCG. The amino acid sequence of both sub units was established in 1975 by Francis Morgan and colleagues at Columbia University, New York.

In 1929, Aschheim using the A-Z bioassay reported greatly elevated urine HCG results in two forms of gestational trophoblastic disease (GTD), choriocarcinoma and hydatidiform mole and in these cases urines often required 1/200 dilution. Choriocarcinoma was first described in Germany by Hans Chiari in 1877 with histological studies reported by M Saengers (1889) and six years later by Felix Marchand. It appears hydatidiform mole was recognised in ancient medicine but described in more detail by Madame Boivin in 1827, who recognised that the hydatids are grape like cystic dilatations of the chorionic villi. Tumours of trophoblastic origin may arise in the uterus, placenta or gonads and tend to be highly malignant and may spread to the lungs and brain. Gestational choriocarcinoma (GC) is rare and occurs in 1/20-50,000 pregnancies, according to conflicting studies, but prior to the 1950s treatment was limited to surgery and radiation and the prognosis was poor. GC has a special place in cancer history, as it was the first condition successfully treated by chemotherapy when in 1958 Roy Hertz and Min Chiu Li at the National Institute of Health, Maryland developed the use of the folic acid inhibitor, methotrexate with great success.

Clinical applications of HCG as tumour marker

The most often adult quoted reference range for serum HCG is <5 IU/L. Serum HCG is used in the follow up and monitoring patients with GTD with extremely high values often exceeding several million IU/L, also in follow up very high



Above. Computer model of the crystal structure of a molecule of human chorionic gonadotropin

IMAGES: SCIENCE PHOTO LIBRARY/ALAMY

results may indicate treatment failures. HCG concentration tends to correlate with tumour volume allowing accurate titration of chemotherapy. The most adult quoted reference range is <5 IU/L.

Serum HCG in combination with AFP and Lactate dehydrogenase is recognised as the best validated prognostic markers for diagnosis, follow up and monitoring germ cell tumours (seminomas, NSGCT and extragonadal tumours).

It is important to distinguish seminomas from teratomas, as each is treated differently with chemotherapy or surgery respectively. In seminomas HCG may range from 10-2000 IU/L. In NSGCT HCG may range from 5-1000 IU/L and depends on stage of the tumour. CSF HCG is more increased in primary intracranial germ cell tumours compared with serum HCG.

Analysis of HCG

HCG exists in multiple forms in serum as intact HCG, Free Beta subunit, Beta core fragment, nicked HCG and hyperglycosylated HCG. Consequently, when used as a tumour marker the HCG assay should detect all main forms, and laboratories should be aware of the characteristics of the assay in use in clinical interpretative medicine. The Beta core fragment is the main form in urine but hyperglycosylated HCG is main urine form in early pregnancy.

The AZ urine HCG test was used extensively with a number of modifications, most notably in 1941 by Eleanor Delfs, the distinguished professor of Obstetrics at Johns Hopkins University and later pioneer HCG researcher at Wisconsin Medical College. Delfs developed a serum HCG bioassay injecting serum extracts into female rats and measuring uterine weight.

Bioassays continued until the first immunoassays were developed in 1960, this followed the typical development pattern of peptide immunoassays with first complement fixation and in the same year an haemagglutination inhibition assay for urine HCG devised by Lief Wide and Carl Gemzell in Stockholm, the reactants were incubated in tubes for two hours and read visually. In 1962, a group led by Jennifer Robbins developed a similar latex agglutination method version using coated latex beads for urine HCG. The Gravindex pregnancy test was based on this latex agglutination inhibition principle.

The pioneering work laid the foundations for two of the most useful tumour markers to date

In 1965, a radioimmunoassay was developed by a team at Charing Cross Hospital Medical School, led by CE Wilde. Charing Cross became a major oncology centre for GTD under the leadership of Prof Kenneth Bagshawe during this period and in 1969 he reported an improved HCG radioimmunoassay. Charing Cross was also notable for pioneering chemotherapy agent developments, including multidrug combinations under the leadership of Edward Newlands, in GTD, testicular, ovarian cancer and brain tumours.

Early commercial kit methods for urine HCG using the agglutination methods were compared and critically reviewed by Derek Watson in 1966 and found to be suitable for detection and monitoring GTD. In 1972, a radioimmunoassay specific for beta HCG was developed and was shown to be clinically useful in monitoring chemotherapy in GTD and follow up of terminated molar pregnancies. The introduction of monoclonal antibodies into immunoassays from 1975 led to a range of two antibody immunometric assays using high sensitivity fluorimetric and chemiluminescent tracer detection assays developed over the last few decades. Reported potential sources of error include lack of specificity-some trophoblastic tumours secrete nicked HCG which is not measured in all assays, due to the very high HCG concentrations often encountered the "high dose hook" effect produce falsely low results and samples require dilution. In addition the presence of heterophilic antibodies may cause errors. Point-of-care and commercial devices for urine pregnancy testing generally are based on a sandwich ELISA dye detection principle and are qualitative only, it is essential they detect hyperglycosylated HCG.

Concluding comments

AFP and HCG have been shown to be remarkable glycoproteins with combined importance in Down's syndrome screening in maternal serum and in monitoring NSGCT. Serum AFP is the first line tumour marker in HCC and serum HCG measurements are essential in the management of GTD.

The pioneering work of the scientists, Abelev and Tatarinov, and Aschheim and Zondek, laid the foundations for their use as two of the most useful tumour markers to date. IBMS

Stephen Clarke is a retired IBMS Fellow. He previously worked in clinical chemistry at Southmead Hospital, Bristol.

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

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Jo Horne, **Andrew Usher** and **Gerry van Schalkwyk** discuss the progress of the histopathology reporting programme and look to the future.

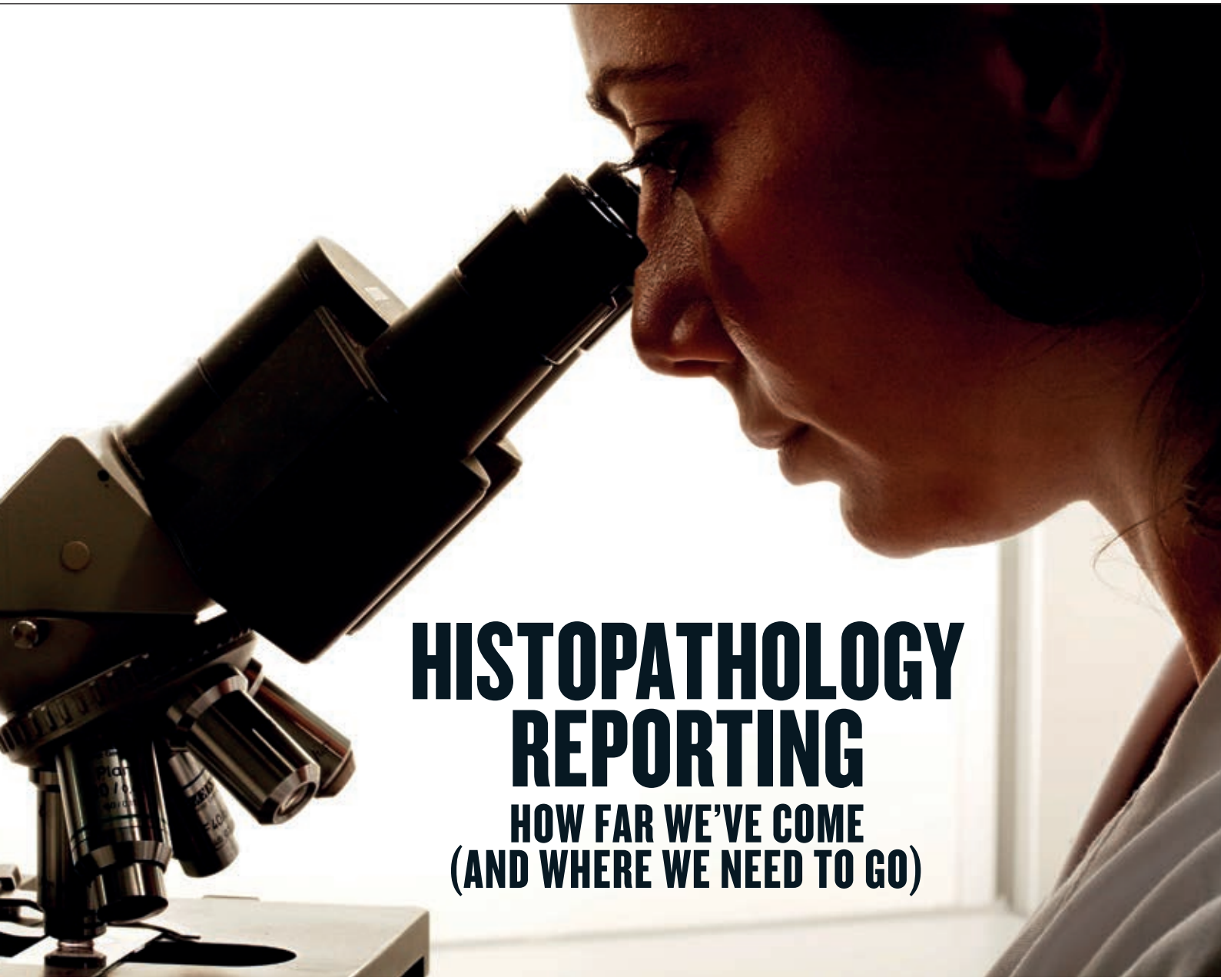
It has been six years since the histopathology reporting programme started in the UK. For many years it has been clear that there are workforce issues within histopathology, with a lower than optimal fill rate of training posts and a large proportion of the pathologist workforce due to retire in the next five years.

In 2010 a working party from the Royal College of Pathologists (RCPath) and the IBMS began to develop a pilot project to seek to train a cohort of biomedical scientists to report gastrointestinal or gynaecological histopathology specimens.

These specialties were chosen as they were large volume, with gynaecology especially targeted as a pathway that cytologists could follow. This small group of histopathologists and biomedical scientists drove forward the pilot programme, by writing a curriculum based on the histopathology curriculum for medical trainees, assessing portfolios and running the practical examinations.

The first cohort of trainees began the pilot programme in September 2012, and at the end of the first year a small group of trainees sat the first ever practical competency exam at the RCPath in London, comprising of slide stations with report writing, assessment of macroscopic images and face-to-face examination by consultant histopathologist assessors.

These trainees came from diverse backgrounds, such as advanced practitioners in histological dissection, laboratory managers and consultant biomedical scientists in cytology. The first year was a success, as a number of these trainees passed their portfolios and the competency exam, and within two years



HISTOPATHOLOGY REPORTING

HOW FAR WE'VE COME (AND WHERE WE NEED TO GO)

IMAGES: GETTY/SCIENCE PHOTO LIBRARY

of the pilot commencing, it became a fully established training programme in 2014, with the formation of a conjoint RCPath and IBMS board.

Candidate success

Each year has seen a new influx of trainees into the reporting programme, with currently more than 50 at various stages within the programme. Some have been successful, whilst others have faced a variety of barriers precluding their success, resulting in them leaving the programme. These barriers, including management of existing roles, and a lack of support, time and backfill, were identified as part of a trainee survey and discussed in a previous article in *The Biomedical Scientist*.

From the original group of trainees, five attempted the first sitting of the stage C exam in 2015. The exam was run over two days in Leicester, and was mirrored on the FRCPath part two exam, but excluded frozen sections and diagnostic cytology. The examination comprised 20 short cases, four long cases, four macros (assessment and discussion around macroscopic photographs) and two Objective Structured Practical Examinations (OSPEs), involving written and face-to-face discussion of management or theoretical issues. One candidate passed the stage C exam, and more followed within the next 12 months.

When medical trainees pass the FRCPath part two, they then undergo a period of further competency-based training within their training laboratory before being awarded their Certificate of Completion of Training (CCT), with the decision made at their Annual Review of

Competence Progression (ARCP) meeting. For scientific trainees, there is also a CCT at the end of stage D, but there is currently no formal ARCP. Additional specific structure and guidance had to be implemented for scientific trainees to be allowed to progress and for consultant histopathologists to accept the validity of the training programme, when compared to that of medical trainees. The stage D guidance for the histopathology reporting programme was written in 2016, and the two trainees who has passed the exam by this point began independent reporting.

Programme development

Another important step in programme development occurred in 2016. The examination process was formally absorbed into the RCPath examinations department. This meant examinations were set and assessed by RCPath examiners, papers were centrally marked and examinations began to run annually, in parallel with other histopathology examinations for medically qualified trainees. The stage A exam is now at the same time as the ST1 resit examination in June, while the stage C exam takes place at the same time as the autumn FRCPath part 2 exam. Trainees apply for the exam and are informed of the outcome via the RCPath website, like any other trainee. These steps have been important for the reporting programme, as although they may seem like simple practicalities, they send a clear message about validity and standardisation of the qualification.

In 2017, the first two trainees achieved their CCT and the dermatopathology pathway was introduced, with a number of new trainees choosing this route. One of these trainees is a Scientist Training Programme (STP) graduate clinical scientist, thus opening up further opportunities for scientists from all training backgrounds within histopathology departments. Another milestone was reached in 2017, as the first consultant biomedical scientist in histopathology reporting was appointed, and no doubt more will follow within the next few years.

TIMELINE OF THE HISTOPATHOLOGY REPORTING PROGRAMME PROGRESS SO FAR.

2010
- Working party from the RCPath and IBMS begin to develop the histopathology reporting pilot

2012
- First cohort of scientific trainees enter the histopathology reporting pilot programme

2013
- First sitting of the end of stage A competency exam ination

2014
- Qualification becomes a full training programme
- RCPath and IBMS Conpint Board formed

2015
- First sitting of the end of stage C exam ination
- First trainee passes the stage C exam ination

2016
- Stage D independent reporting guidance written
- Exam inations absorbed into RCPath system with central marking and ratification
- First trainees begin formal stage D and independent reporting

2017
- First trainees awarded CCT
- First consultant level post created
- New dermatopathology module offered
- First STP graduate enters training programme

2018
- Development of new modules under consideration

Looking forward

So, where are we in 2018? One of the most important roles for those of us involved in histopathology reporting is to get out there and promote the qualification and the opportunities that it can deliver. It is now about winning the hearts and minds of the wider histopathology community, and to develop appropriate consultant level posts for successful trainees to move into after CCT, either within their existing department, or at other trusts. The qualification can provide many opportunities – for the trainee, consultants, other colleagues within the laboratory, the organisation and, most importantly, the patient.

Six years on from the start of the reporting pilot, we continue to look to the future. Histopathology is evolving, in terms of workload and new technologies, such as genomics and digital pathology. The workforce also needs to adapt and develop to meet these future needs. We need to look at the introduction of new pathways into the reporting qualification, perhaps in the long term considering a generic early qualification before specialisation into one area. But we must develop this with our colleagues within all stakeholder organisations, so that in the long term there is a clear and standardised pathway of training in histopathology reporting for any trainee wishing to specialise in this area, whether their background is as a medic or a healthcare scientist. BMS

Jo Horne is an Advanced Practitioner Healthcare Scientist in Cellular Pathology at Southampton General Hospital.
Andrew Usher is Cellular Pathology Laboratory Manager at Cheltenham General Hospital.
Gerry van Schalkwyk is a Consultant Histopathologist at the Royal Derby Hospital.

HOW TO...
#COMMUNICATE THROUGH SOCIAL

After creating videos to highlight pathology's role in patient care, **Claire Kennedy** and **Rachel Berkoff** explain why they used social media to communicate their messages, and offer tips and advice on how to make the most of the medium.

One of the key aims for many people using social media is to engage and connect with other people and share their passions and interests. Social media channels, such as Twitter, can also be a fantastic learning and education resource.

Whatever your interest in pathology you will find someone on social media to connect with or to follow. You can follow organisations, experienced pathologists and biomedical scientists based in the UK and abroad, as well as those just starting their professional careers.

Many healthcare leaders and organisations have social media accounts, including the IBMS and its Chief Executive Jill Rodney, and the Royal College of Pathologists and its President Jo Martin. In addition, there are many high-profile scientists, politicians, business leaders and academics that use social media.

Think about which social media channels you would like to use and why. South West London Pathology uses Twitter, LinkedIn and YouTube as key social media channels with the aim of sharing information about pathology, highlighting our work as one of the leading NHS pathology providers in the UK, and as a recruitment tool.

The Royal College of Pathologists uses Twitter, Facebook and YouTube as their main social media channels to communicate to the general public as well as their members. A key objective of the College is to help to explain to the general public what pathology is, and why it matters. Social media is a great tool for getting this message across by engaging with other relevant organisations and stakeholders and showing how pathology can relate to these.

Be aware

If you want to get more involved in using social media, find out if your organisation has any social media guidelines or a social media policy in place. This may give you advice about what to consider if you would like to use social media. It is likely to cover what is appropriate and inappropriate to post, which channels to use and why.

If your organisation doesn't have any social media guidelines, many health organisations, such as Healthcare Professions Council and NHS Employers, have guidance.

Remember – any social media policy will not cover every scenario, so think before you post.

When photographing or filming in a laboratory, there will be lots of patient data. Make sure that none of it can be seen before you post.

A collaborative project

Up to 70% of all patient diagnoses depend on pathology, however, pathology is often considered a "back office" service.

In addition, due to the sensitive and confidential nature of the work, processing pathology samples takes place behind closed doors with restricted access. Most people (including most healthcare

MEDIA

SOCIAL MEDIA TOP TIPS

- **If you're not sure which social media channel to use, set up a dummy account and try the channel for six weeks and see if you like it.** This will allow you to have a look at other accounts, see what's being posted and how others use the channel.
- **Knowing what your goals are will help you to determine which channel might be best for you, who to follow, what to post and why.** For example, do you want to raise your professional profile, keep track of certain issues, or to just share information?
- **When you find an account you like, ask yourself why you like it?** Being able to pinpoint what you find useful or interesting will give you ideas for your own posts.
- **If you're using Twitter, use hashtags to promote your posts so people can find related tweets** – in our social media posts we used #DiscoverPathology
- **Post regularly** – even if it's just sharing information you've read on another post. Allocate time every day or week to review social media activity and post, share or add comments to other posts.

professionals, as well as the general public) are unaware of what happens in a hospital pathology laboratory.

South West London Pathology applied for a public engagement grant from the Royal College of Pathologists. Instead of offering money towards producing the videos, the college thought it would be a really good opportunity to work on the project together. One of the things both organisations were really keen to highlight was the expertise involved in making diagnoses, and the role of pathologists in patient care. Many other organisations also offer grants for public engagement activity, including the IBMS.

Achieving aims

The aim was to use social media in an engaging way to raise the profile of pathology and show how essential it is to the patient pathway. South West London Pathology regularly hosts public engagement events and provides laboratory tours to hospital staff, members of the public, students and VIPs. These events always receive positive feedback and a video was one way to show parts of a laboratory tour in a visual and accessible format.

The videos (still from which are pictured, left) follow each stage of the journey of the sample, from the courier who brings the sample to the hospital, to the biomedical scientist who stains it to the consultant who looks at it under the microscope.

As well as explaining the process, the videos also highlight and celebrate the many people involved in every test. This was great for social media: focusing on the people in the lab, and why they were there, rather than just what they were doing was a great way to engage with our audience.

We decided to use video as it is a quick and descriptive way to explain what was happening. Video is particularly popular on social media, and with regard to something like the laboratory, where the general public are not usually allowed access, it allows the viewer to see and hear something they may not have ever been able to.

We have posted the first two videos onto our social media channels and we're also aiming to reach a wider audience by working with other NHS organisations, universities, health charities and local health organisations to share and promote the videos. If you would like to watch the videos yourself, just search #DiscoverPathology on Twitter. BMS

Claire Kennedy is Communications Lead at South West London Pathology and **Rachel Berkoff** is Communications Team Administrator at the Royal College of Pathologists.

MY IBMS NEWS

IBMS AGM

MEMBERS AWARDED PRIZES

Each year the IBMS AGM sees a number of awards and Company Members' prizes given to promising scientists.

These prestigious prizes go to the biomedical scientists who have shown excellence in their fields of study over the course of the year.

The Company Members' Prize of the Higher Specialist Diploma (HSD) is awarded to the candidates who in their first attempt, earn the highest mark in each discipline of the Higher Specialist Diploma examination. This year's awards go to:

- **Sandra Iles** from Hammersmith Hospital in London for the Higher Specialist Diploma Company Members Prize in Cellular Pathology
- **Joanne McCauley** from Edinburgh Royal Infirmary for the Higher Specialist Diploma Company Members Prize in Clinical Chemistry
- **Alena Charnetski** from St George's Hospital in London for the Higher Specialist Diploma Company Members Prize in Cytopathology
- **Susan Jeffrey** from Dumfries and Galloway Royal Infirmary for the Higher Specialist Diploma Company Members Prize in Haematology
- **Penny Feather** from the Northern General Hospital in Sheffield for the Higher Specialist Diploma Company Members Prize in Immunology
- **Faye Teare** from the Royal Victoria Infirmary in Newcastle-upon-Tyne for the Higher Specialist Diploma Company Members Prize in Leadership and Management
- **Lesley Davies** from NHS Blood and Transplant in Newcastle-upon-Tyne for the Higher Specialist Diploma Company Members Prize in Transfusion Science
- **Shireen Padayachy**, from Southampton General Hospital who achieved the highest mark across all Diploma of Expert Practice qualifications in Histological Dissection.

The RJ Lavington Prize consists of a cheque for £500 and a medal and is awarded to the candidate who receives the highest mark across all disciplines.

This year's award was presented to Alena Charnetski, who undertook the Higher Specialist Diploma in Cytopathology.

IBMS President Alison Geddis said: "These awards are made in recognition of individual achievement, and these candidates have demonstrated their excellence in the field. Well done to the all the candidates."

BIOMEDICAL SCIENCE DAY

Funding for promotion

A high number of responses lead to an increase in funding for Biomedical Science Day 2018.

To help members celebrate on 19 July, the Albert Norman Trust Fund agreed to release funds for members wishing to develop their public engagement activities. Members were encouraged to apply, with up to £500 available for each successful application.

As a high number of excellent applications were received that met the criteria, additional funds were released to meet the demand.

There were 23 successful applications for funding, with activities ranging from lab tours and demonstration to microbe games and dissection kits for children.

→ **For more information, visit biomedicalscienceday.com**

INTERNATIONAL

DEVELOPING A SOLAR DIGITAL LIBRARY FOR AFRICA

The IBMS has donated documents to a Master's student project to provide a low-cost digital library for hospital technicians in Rwanda and Tanzania.

Sarah Patterson, from Arizona State University, is conducting the project in collaboration with Engineering World Health and Arizona State University's SolarSPELL.

The digital library requires no internet connection or electricity and holds more than 1,600 resources.

COUNCIL ELECTIONS

The results of the 2018 IBMS Council elections were announced by the President at the AGM in Belfast on 9 June 2018.

National

There were two national Council vacancies this year. Mr Sean Conlan and Mr Daniel Smith were due to retire at the close of the AGM.

Four candidates stood for election and Mr Sean Conlan and Mr Daniel Smith were duly elected by ballot, and took office from the conclusion of the AGM and will serve for a term of three years.

Regional

Five regional members were due to retire at the close of the AGM, namely, Mr Colin Mudd (East Midlands), Mr David Wells (London), Mrs Debra Padgett (North East), Mr David Eccleston (North West) and Mr Matthew Smith (East Anglia).

Nominations for the vacancies were received from Mr Colin Mudd (East Midlands), Mr David Wells (London), Mrs Debra Padgett (North East) and Mr David Eccleston (North West) and they were duly elected regional members of Council, without the requirement for a ballot, and took office from the conclusion of the meeting for a term of three years.

Three nominations for the East Anglia vacancy were received and Mr Matthew Smith was duly elected by ballot, and took office from the conclusion of the AGM and will serve for a term of three years.

OBITUARY

ANTHONY J HARDING (1944-2018)

The Institute received notification recently of the death on 14 April of Life Member Anthony (Tony) J Harding, aged 73.

Tony commenced full-time laboratory work in May 1961, at the Queen Elizabeth Hospital for Children on Hackney Road, East London, subsequently registered as a student member of the Institute in October 1963, and passed the Examination for Ordinary Membership in 1964. He then achieved Institute Associateship in 1967 following success in the Final Examination in Haematology, and gained Fellowship in 1979 after success in the Final Examination in Parasitology.

During his career, Tony served as secretary of the Institute's Cleveland branch and North region before his election to Council in 1986, on which he served until 1992. During his two three-year terms, he was a member of a number of Institute standing committees, including Finance, Science, Publicity and Management. Tony was particularly astute in matters of revenue generation and laboratory management, and was a longstanding chairman of the Management Advisory Committee. He was awarded Institute Life Membership in 1999, shortly after retiring from his post as Divisional Manager of Pathology at South Tees NHS Trust in Middlesbrough.

Tony was a keen gardener, particularly in the Japanese style, and had a love of classic cars, especially the Marcos that he and his wife, Brenda, restored. History was also close to his heart, and this was manifest in his interest in local Teesside history as well as that associated with the professional body to which he had devoted much time, both before and after retirement.

Tony's interest in Institute history dated back to 1978, when he joined the History Committee (then Historical Section) acting as its chairman from 2003 to 2014. He was also a founder member of the Medical Sciences Historical Society.

In the run up to the Institute's centenary in January 2012, Tony, David Petts and Brian Nation were approached by Alan Potter (then Chief Executive) to consider writing a new book charting the Institute's history. Several years of intense research, investigation, travel and writing followed, and Letters of Consequence: A History of the Institute of Biomedical Science was delivered to the Institute's office in late November 2011.

The size and content of Tony's professional file at the Institute's office is testament to the commitment, dedication and energy that he displayed both throughout his professional career and into retirement. He will be sadly missed as a friend and colleague, and a source of wise counsel.

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 3 OCTOBER 2018

Idiopathic inflammatory myopathies – a guide to subtypes, diagnostic approach and treatment. Oldroyd A, Lilleker J, Chinoy H. *Clin Med (Lond)* 2017; **17** (4): 322–8. Assessment No: 070518

01	A 9–19% frequency of anti-SSA autoantibodies has been reported in adult PM/DM overlap cases, compared with 14–25% in IIM-non-overlap cases.
02	Immune-mediated necrotising myopathy (IMNM), a rare but severe IIM subtype, is characterised by muscle necrosis and regeneration resulting in proximal muscle weakness.
03	IMNM is also associated with presence of the anti-signal recognition particle autoantibody.
04	Coexisting IIM and mixed CTD is associated with positivity for anti-U1-snRNP autoantibodies, which confers a poor response to steroid treatment and increases prevalence of myositis.
05	For individuals with moderate disease severity, oral prednisolone at a dose of 5–10 mg/kg/day is recommended.
06	Testing for myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) can further identify clinical subtype, inform the requirement for further investigations and predict treatment response.
07	The anti-PM/Scl autoantibody occurs most commonly in patients who have PM with overlapping sclerodermatous features.
08	Identification of MSA/MAAs can inform diagnosis and risk of secondary organ involvement and cancer development.
09	Dermatomyositis (DM) can be distinguished from PM by its typical cutaneous features, which include Gottron's papules, Gottron's sign, heliotrope rash, V-sign rash, mechanic's hands, shawl sign rash and erythroderma.
10	Patients positive for the anti-Ku autoantibody are more likely to suffer Raynaud's phenomenon, ILD, arthralgia and myositis.
11	Although a raised CK is sensitive for a diagnosis of an IIM, there are many other causes of a raised CK.
12	Features particular to juvenile DM include cutaneous ulcerations, calcinosis cutis and vasculopathy.
13	Gottron's sign consists of red, scaly papules that occur over the dorsal aspect of the metacarpophalangeal, proximal and distal interphalangeal joints, whereas Gottron's papules are the same red, scaly papular rash occurring elsewhere on the body.
14	25% of anti-synthetase antibodies are Jo-1.
15	The statin-associated form of IMNM is associated with autoantibodies directed against HMGCR and characteristically improves following withdrawal of the statin.
16	The anti-synthetase syndrome is a particularly severe IIM subtype associated with myositis, ILD and inflammatory symmetrical polyarthritis of the small joints of the hands and feet.
17	TIF1 is seen in 3–13% of adult PM/DM with a strong association with cancer.
18	Fever, Raynaud's phenomenon and mechanic's hands are also characteristic of the anti-synthetase syndrome.
19	Treatment with tacrolimus, cyclosphosphamide, rituximab, tocilizumab or intravenous immunoglobulin can also be considered under specialist care for more resistant cases.
20	The risk of cancer in the IIMs is between two and seven times higher than in the general population.

Characterisation of the scope and magnitude of biotin interference in susceptible Roche Elecsys competitive and sandwich immunoassays. Trambas C, Lu Z, Yen T, Sikaris K. *Ann Clin Biochem* 2018; **55** (2): 205–15. Assessment No: 070318

01	The binding between biotin and streptavidin is very strong.
02	High-dose biotin therapy is rarely used and is likely to become less common in the future.
03	Generally, sandwich immunoassays will give lower results when samples contain high levels of biotin.
04	The data in the paper suggest the biotin interference in sandwich immunoassays is independent of analyte concentration.
05	Prolactin levels in samples containing 0.5 mg/L biotin are around 30% of those without biotin spiking.
06	A normal female testosterone level would be increased to that associated with PCOS with biotin levels of 500 µg/L.
07	Biotin metabolites bind to streptavidin with equal affinity to biotin.
08	To assist in the interpretation of these findings, studies of biotin pharmacokinetics are warranted.
09	Biotin therapy or use will only be an issue in a clearly defined group of patients.
10	Renal insufficiency is likely to exacerbate the effects of biotin therapy.
11	It may take about a week for measured anti-TSH receptor antibody levels to return to the true value.
12	This study would be almost impossible to conduct in samples naturally containing high levels of biotin.
13	*In vivo* indicates experiments that take place in a reaction vessel.
14	The effect on TSH and free T4 does not mimic any common clinical condition.
15	Low-dose biotin supplements are unlikely to mask pregnancy assessed using serum β-hCG measurements.
16	Normal plasma biotin levels are around 0.5 µg/L.
17	This issue only concerns Roche platform users.
18	This effect is unlikely to cause any issues with the recommendations for lower troponin levels currently being introduced as an early screen for MI.
19	To date, no serious clinical issues have been reported due to this interference.
20	The effect on PSA is likely to remain clinically insignificant.

REFLECTIVE LEARNING

01	Review the myositis-specific antibodies tested for in your laboratory. How do you make sure you consider those autoantibody profiles that are not tested in your laboratory?
02	Critically appraise the differential diagnosis of idiopathic inflammatory myopathies.

01	Outline a strategy for dealing with this issue in your laboratory and hospital. Would this make any difference if you were serving a regional neurology centre?
02	What other commonly available nutritional supplements and herbal medications can affect endogenous metabolite and therapeutic drug levels?

EVENTS AND TRAINING COURSES

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

DATE	TITLE	VENUE CONTACT
July		
2 – 5 Jul	**Identification of pathogenic fungi**	Bristol I michael.palmer@phe.gov.uk
4 Jul	**HPLC method development**	Reading, York, Scotland, London and Manchester I jsumner@hichrom.com
4 Jul	**Urinary cytology**	Bristol I SWRCTC@nbt.nhs.uk
6 Jul	**WMA Summer Meeting 2018**	Swansea I kirsten.winterburn@wales.nhs.uk
8 – 11 Jul	**Light microscopy summer school**	York I katejermey@rms.org.uk
10 Jul	**Introduction to blood cell morphology 2018**	Manchester I I.ahmed@mmu.ac.uk
11 – 12 Jul	**Essentials in microscopy**	Southend on Sea I debby.dawson@olympus.co.uk
12 Juy	**SHOT Symposium 2018**	Manchester I SHOT@NHSBT.NHS.UK
12 – 13 Jul	**Getting the most from your confocal course 2018**	York I katejermey@rms.org.uk
13 Jul	**Northern autoimmunity education and quality assurance group**	Preston I fiona.nash@lthtr.nhs.uk
15 – 20 Jul	**Electron microscopy summer school**	Leeds I katejermey@rms.org.uk
18 – 20 Jul	**Flow cytometry course**	Edinburgh I katejermey@rms.org.uk
27 Jul	**Employer Forum Annual meeting**	London I I.mattarini@westminster.ac.uk
27 Jul	**Train the trainer**	London I fstshortcourses@westminster.ac.uk
August		
1 Aug – 17 Sep	**UK NEQAS Cellular Pathology Technique tissue morphology and recognition workshop**	Gateshead I chantell.hodgson@nhs.net
21 – 23 Aug	**Standardized susceptibility testing – residential workshop 2018**	Cardiff I dirwin@bsac.org.uk
September		
4 – 6 Sep	**Three-day update for cervical cytology**	Bristol I SWRCTC@nbt.nhs.uk
11 Sep	**Mycology teaching workshop**	London I organiser@ukneqasmicro.org.uk
12 Sep	**Mycology teaching workshop**	London I organiser@ukneqasmicro.org.uk
12 – 13 Sep	**UK NEQAS Cellular Pathology Technique Mohs/BMT/renal workshop**	Gateshead I chantell.hodgson@nhs.net
13 Sep	**Mycology teaching workshop**	London I organiser@ukneqasmicro.org.uk
21 – 22 Sep	**Advanced course in EBUS/mediastinal EUS and rapid on-site evaluation for chest physicians and cytopathology teams**	Watford I winnie.tang@whht.nhs.uk
28 Sep	**Update course in gynaecological cytology – MDT cases and squamous lesions**	Birmingham I amanda.lugg@bwnft.nhs.uk

DATE	TITLE	VENUE CONTACT
October		
4 Oct	**ISO Accreditation for POCT October 2018**	Leicester I nichola.cadwallader@sbk-healthcare.co.uk
8 – 12 Oct	**Introduction to the principles and practices of working safely at ACDP containment Level 3**	Porton Down I nadp.training@phe.gov.uk
9 Oct	**HPLC troubleshooting**	Reading, Scotland, Manchester I jsumner@hichrom.com
10 Oct	**HPLC method development**	Reading, York, Scotland, London, Manchester I jsumner@hichrom.com
17 Oct	**One-day update in cervical cytology audit**	Bristol I SWRCTC@nbt.nhs.uk
17 Oct	**UK NEQAS Cellular Pathology Technique tissue morphology and recognition workshop**	Gateshead I chantell.hodgson@nhs.net
18 Oct	**UK NEQAS Cellular Pathology Technique Tissue Preparation Techniques Workshop**	Gateshead I chantell.hodgson@nhs.net
22 Oct	**Update course in gynaecological cytology – HPV update and glandular lesions**	Birmingham I amanda.lugg@bwnft.nhs.uk
November		
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 – 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
12 – 16 Nov	**Biosafety practitioner Level 1 (ISTR accredited)**	Porton Down I nadp.training@phe.gov.uk
14 Nov	**FNA cytology**	Bristol I SWRCTC@nbt.nhs.uk

HERE TO HELP

RE-EVALUATING AND REFLECTING

Jocelyn Pryce, Head of Registration and Training at the IBMS, explains the checks required to register.

Regular readers of this column will know that here in the education department we are continuously reviewing our processes to ensure that they are as streamlined as possible and fit for purpose for all concerned. Almost all of those changes are driven by the recognition that, with the staff and workload profiles changing within laboratories and the significant increase in demands for our services, we must work with our service users to create processes which make good and effective use of all of our time. Our aims are to make the various requirements we have achievable in the most painless way possible and we are constantly re-evaluating and reflecting to make sure this is the case.

Occasionally, however, we may have to make a change that could seem counter-intuitive to these aims. An example of this is a requirement that has been introduced in a more formal way recently for those applying to join our various routes to registration; disability and barring service (DBS) checks. These checks are also known as criminal record bureau checks (CRB) and protecting vulnerable groups (PVG) checks. Some of you will have noticed that on our numerous application forms we now have a more formal requirement of a declaration that a DBS check has taken place.

We have had to implement a more robust process for ensuring checks have taken place as part of our requirement to meet the HCPC Standards of Education and Training (SETs) for our various routes to registration, in this case SET 2.4. – *The admissions process must assess the suitability of applicants, including criminal conviction checks.*

We did not take the decision lightly, as we are aware that it places more responsibility onto the candidates, training teams and employers. However, we must be assured that anyone undertaking our routes to registration meets these requirements. The HCPC has highlighted this as a potential concern should a candidate have travelled all the way through the process to the point of application for registration and the criminal conviction coming to light. This could be viewed as a possible barrier to them being eligible to register and seen as an oversight on the part of the education provider not to have highlighted it earlier in the process. In response to this, we now check at the point of application and again at the point of issuing the Certificate of Competence, so that we can satisfy the requirements of the HCPC both at the outset of their journey and at the point where we would normally expect them to apply for registration. Our approach is to raise awareness of it at the point of application so that candidates can be directed straight to the HCPC for guidance should something appear on the DBS check. We will also confirm once again at the point of award of the certificate that nothing has changed in the interim. This will demonstrate that we are exercising a duty of care as the education provider, to our trainees to ensure that they can meet this requirement of registration.

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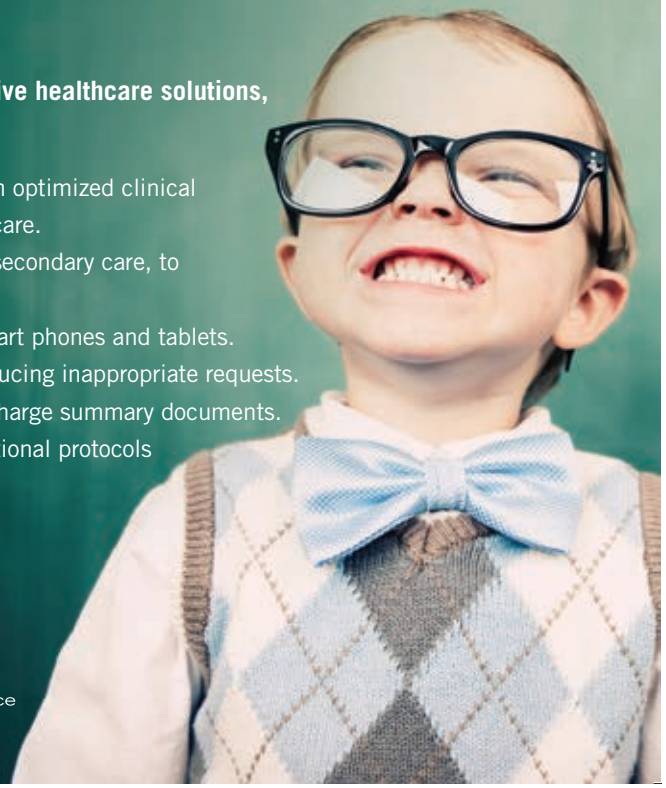

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MY LAB

POINT-OF-CARE LABORATORY

Michelle Lineham, Deputy Team Lead and Biomedical Scientist, gives a guided tour of her lab at Addenbrooke's Hospital in Cambridge.

The point-of-care testing (POCT) team at Addenbrooke's Hospital (Cambridge University Hospitals NHS Foundation Trust) consists of 24 members of staff, consisting of biomedical scientists, associate practitioners, and administration staff, providing diagnostic testing outside of the conventional laboratory, the majority of which is at the patient bedside.

We also have small POCT laboratories in both the emergency department (ED) and oncology to provide fast turnaround times on routine tests, to enable more efficient discharge, or aid quicker decisions on treatment, such as chemotherapy for oncology patients. These laboratories are staffed by our own team, rather than end-users, and the ED lab is a 24/7 service. We also provide ward-based POCT devices, such as glucose meters, INR meters and gas machines, among others, and provide support in the use of these through maintenance, provision and monitoring of EQA and continual training on devices to ensure competence of end-users. As a team, we are also often asked to evaluate new devices and the repertoire of POCT at Addenbrooke's is expanding rapidly, as more wards are asking for advice on POCT as an alternative to laboratory testing.

My team is heavily involved in training of end-users, giving presentations at induction to each new intake of qualified staff, which can range from groups of 70 to 100, and training in smaller groups and one-to-one, where necessary.

As a department, we recently gained IBMS accreditation as a training laboratory for the certificate of competence, so that we could begin to take on trainee biomedical scientists and train them in POCT as a stand-alone "laboratory" service.

In the last year, we were able to take on our first trainee biomedical scientist, who successfully gained her certificate of competence in April. Working in the POCT department is very challenging and unpredictable, which can involve a lot of day-to-day problem solving. With the trust relying heavily on POCT, we provide an on-call out-of-hours service to ensure continuous provision of a high quality service.

We are also involved in evaluation projects of POCT devices. During the winter season, I have been involved in evaluating POCT PCR devices for flu in comparison to the central laboratory method, in order to provide a PCR analyser at the point-of-care for ED. This would mean that patients testing positive for flu can be isolated more quickly to help minimise the spread and outbreak of flu within the hospital. In the near future, we are also hoping to evaluate POCT devices for ammonia testing.

I am also hoping to be able to produce a POCT Specialist Portfolio that our biomedical scientists can complete as part of their CPD. In addition, we are working towards moving the majority, if not all, of our refresher training to e-learning packages to ensure efficiency and confidence in the continuous competence of end-users. The aim is also to work towards UKAS accreditation for the POCT service as a whole. BMS

Michelle Lineham won a You Made a Difference Award in May. This recognises staff who have 'made a difference' to patients, visitors or colleagues.

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