THE BIG QUESTION

COVID-19 VACCINE

We ask three scientists if we will have a vaccine by Christmas: *p.14*

TRANSFUSION SCIENCE

ANNUAL SHOT REPORT

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HOW TO...

PLACEMENTS

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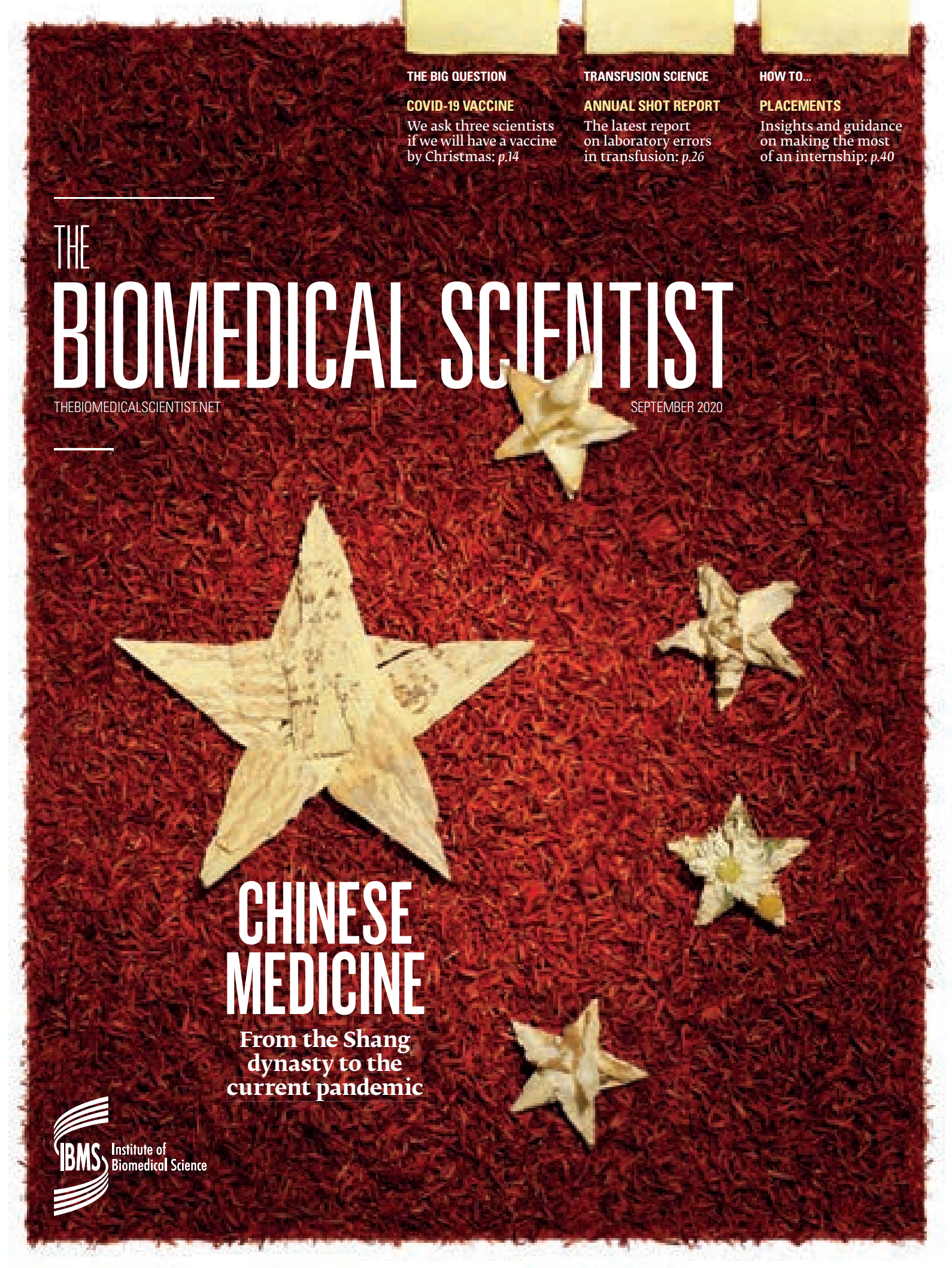
SEPTEMBER 2020



CHINESE MEDICINE

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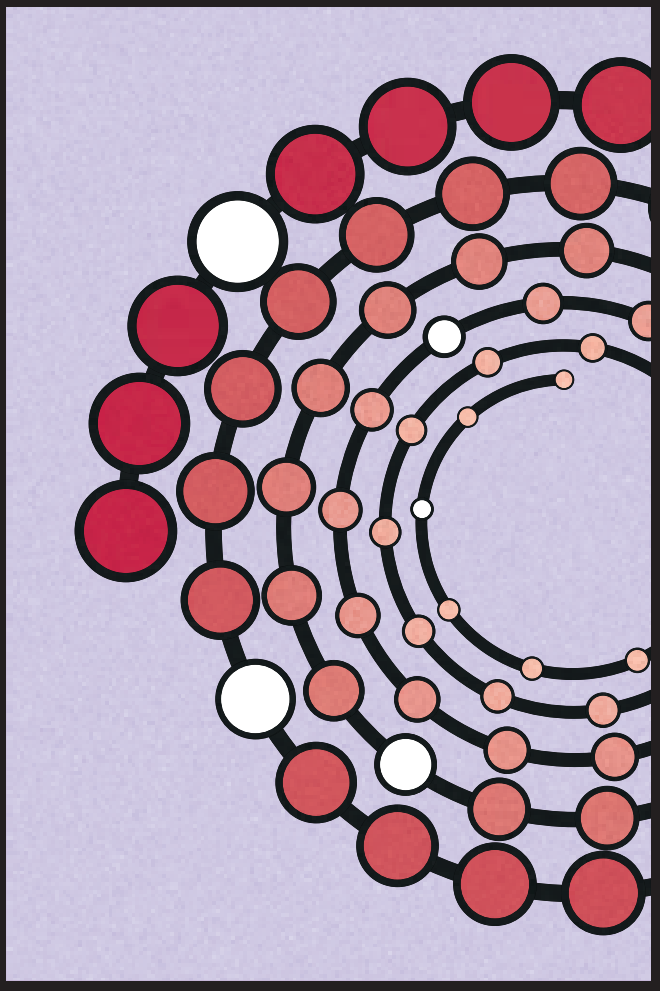

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THE ORGANISATION THAT DELIVERS

After years of frustration, people are finally starting to understand the value of biomedical scientists.

We all know the saying "success breeds success", but I think I'm discovering that confidence also breeds confidence. I'm referring to both our profession and our professional body. Our history is peppered with examples of the frustration of anonymity and, dare I say it, exclusion, but I am detecting a very definite change in the air. The Institute is at last being recognised as a very significant player in the provision of training programmes and qualifications and our profession is seen as a very real part of the solution to the workforce:workload pressures in pathology.

This change has been accelerating over the past couple of years and it is so refreshing after the years of frustrated fighting and fruitless opposition. It feels as though we have been like a complex combination lock where at last all of the tumblers have aligned in the right order and the door opens, but in place of tumblers we have people. Right now, there is the right combination of people with shared goals and the confidence to push through an ambitious agenda that would have been considered a fantasy two years ago.

We are working with Health Education England, The Northern Ireland Pathology Network, the Scottish Government, the National School of Healthcare Science and the Royal College of Pathologists. I don't think we've ever been in a position to report such dialogues; the Institute is at last seen as the organisation that delivers.

But this success isn't down to institutions, it is down to individuals who recognise the need to work together and who have the confidence to challenge and bring about change.

While the coronavirus pandemic has been devastating, it has also brought with it an unexpected benefit for our profession. It has presented the opportunity to inform, clarify and explain about the roles of pathology, scientists and the laboratory services that are key to diagnosis and tracking. We are fortunate that we have strong, articulate people, not least of whom is our President, who have been willing to be interviewed and who have informed journalists, politicians and public alike. To borrow an NHS phrase: we have had the right people, in the right place, at the right time.

Do I think that things will revert back once the COVID-19 crisis is over? No, I don't and I genuinely see new opportunities opening up for us. I am currently in the midst of Congress programme planning and we have decided not to run a molecular pathology lecture stream; not because it is not relevant to our profession, but because it has now become fully integrated across all pathology disciplines – aided not least by COVID testing. Far from our profession being left with the remains of "old school" routine pathology, we are at the heart of new techniques and new services. I promised myself good news, not COVID news, this month. I think I can say "job done".

Sarah May
Deputy Chief Executive

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

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SCIENCE NEWS IN NUMBERS

3.4 million

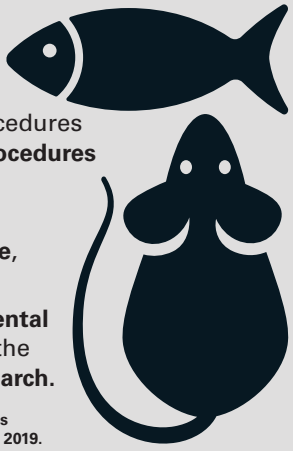
The number of scientific procedures carried out in Great Britain involving living animals in 2019.

3% This represents a **3% decrease** on the number from last year.

51% Around half of all procedures were **experimental procedures (1.73 million)**.

93% The vast majority of procedures used **mice**, **fish**, or **rats**.

57% **Over half of experimental procedures** were for the **purpose of basic research.**



The data comes from the Home Office's Annual Statistics of Scientific Procedures on Living Animals, Great Britain 2019.

CANCER REFERRALS

One in four UK GPs say rising numbers of cancer referrals have been rejected inappropriately during the COVID-19 pandemic.

Around **25% of GPs** said the **proportion of cancer referrals rejected unfairly** during the pandemic increased, compared with last year.

7.5%

death increase in England

ONS data on excess deaths in European countries until the middle of June, compared with the same period last year:

England: 7.5%
UK: 6.9%
Spain: 6.7%
Scotland: 5.1%
Belgium: 3.9%
Wales: 2.8%
Sweden: 2.3%
Netherlands: 2.2%
Northern Ireland: 2%
France: 0.2%

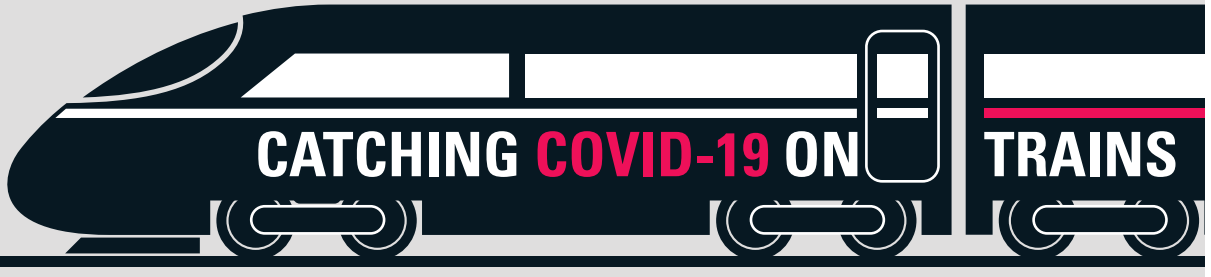
SOCIAL DISTANCING

A new study, published in PLOS ONE, shows the impact that social distancing policies have had. It reveals:

- Such policies have been enacted nationally in **46 countries**.
- They **prevented** an estimated **1.57 million cases of COVID-19.** over a two-week period.
- This represents a **65% reduction** in new cases.

A study by scientists from the University of Southampton examined the chances of catching COVID-19 in a train carriage carrying an infectious person.

For train passengers sitting within **three rows** (width-wise) and **five columns** (length-wise) of an infected person, **between 0% and 10% caught the disease.**



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SCIENCE NEWS

COVID-19

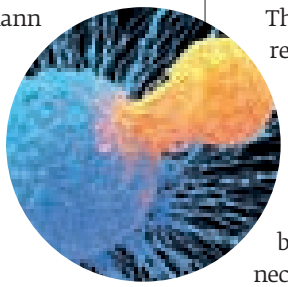
"MORE T CELL DATA NEEDED"

While early research on the adaptive immune response to COVID-19 primarily looked at antibodies, more information is now emerging on how T cells react to the SARS-CoV-2 virus – addressing a crucial knowledge gap.

This claim comes from Daniel Altmann and Rosemary Boyton from Imperial College London in a new paper.

While antibody responses are generally much easier to study, T cells are known to play a more important role in protecting the body against viral infections, in the context of COVID-19.

"Antibody responses appear short-lived and T cell memory is potentially more durable," Altmann and Boyton write. "It's time to admit that we really need the T cell data too."



They state that standardised tests to measure T cell immunity to SARS-CoV-2 could be designed using methods in common with established tests for T cell immunity to *Mycobacterium tuberculosis*.

→ **bit.ly/3hWPqWZ**

DRUG DISCOVERY

Screening to improve mAb-based drugs

By screening potential monoclonal antibody (mAb)-based drugs solely on a measure of their colloidal stability, scientists may be able to weed out mAbs that do not respond efficiently in solution early in the drug discovery process, according to a new study.

This finding could enable researchers to overcome a major hurdle to drug development by identifying promising mAb-based therapies, which must be administered via injection, but often lack the properties necessary to succeed as solutions.

"Therapeutic antibodies that neutralise pathogens are a promising way to treat infectious disease," said Jonathan Kingsbury, study author. "Selection of well-behaved antibodies with molecular properties that enable streamlined manufacturing, scale-up, and subcutaneous delivery is key for rapid development, particularly during a pandemic response."

The paper says mAb solution behaviour can be predicted with 90% accuracy based on its diffusion interaction parameter.

→ **bit.ly/2BOGUKj**

PPE

THREE TIMES RISK FOR FRONTLINE HEALTHCARE WORKERS

Frontline healthcare workers with adequate personal protective equipment (PPE) have a three-fold increased risk of a positive SARS-CoV-2 test, compared with the public.

Those with inadequate PPE had a further increase in risk, while healthcare workers from Black, Asian and minority ethnic (BAME) backgrounds are more likely to test positive.

Using the COVID Symptom Tracker App, researchers from King's College London and Harvard looked at data from 2,035,395 individuals and 99,795 front-line healthcare workers in the UK and US.

The prevalence of SARS-CoV-2 was 2747 cases per 100,000 front-line healthcare workers, compared with 242 cases per 100,000 people in the general community.

A little over 20% of front-line healthcare workers reported at least one symptom associated with SARS-CoV-2 infection compared with 14.4% of the general population.

BAME healthcare workers were at an especially high risk of SARS-CoV-2 infection, with at least a five-fold increased risk of infection compared with the non-Hispanic white general community.

Researchers say their study shows the importance of adequate availability and use of PPE and the crucial need for additional strategies to protect healthcare workers, such as correct application and removal of PPE and avoiding reuse, which was linked to increased risk.

→ **bit.ly/33cTHBu**

IMAGES: GETTY/SCIENCE PHOTO LIBRARY

WHAT'S HOT AND WHAT'S NOT

HOT

CANDY FLOSS

An injectable clotting agent has been created that reduced blood loss by 97% in mice models. The freeze-dried agent has the consistency of candy floss.

HOT

EARLY YEARS

A Centre for Early Life is to be set up at the University of Warwick to investigate issues relating to early life, from before conception up to the age of five.

HOT

TELE CONSULTATION

Health Secretary Matt Hancock said unless there is a clinical reason not to, patients should have teleconsultations with their GPs.

NOT

TICKS

Public Health England is urging people to be alert for tick bites, following the diagnosis for the first time in England of a rare tick-borne illness, babesiosis.

NOT

THE FA CUP

There was no presentation party at this year's FA Cup to minimise the risk of spreading COVID-19.

NOT

DATA SHARING

The failure to adequately share test results has been one of the "biggest omissions" in the handling of the coronavirus crisis, IBMS President Allan Wilson said.

P-TAU217

Blood test for Alzheimer's

A blood test could spot Alzheimer's disease at the earliest stage and years before symptoms appear, new studies indicate.

The test looks for tiny amounts of a protein (p-tau217) that is elevated in people with the illness.

Investigators found measuring this could predict Alzheimer's dementia with 96% accuracy.

Alzheimer's is currently diagnosed using memory tests and brain scans when symptoms have appeared.

The idea of a dementia blood test is not new, but two new studies give the clearest indication yet that a protein associated with Alzheimer's disease could be used to diagnose people at a much earlier stage.

Dr Rosa Sancho, Head of Research at Alzheimer's Research UK, said previous clinical trials had failed as patients enrolled in them were too far advanced in their illness, and by that time it was "too late".

→ **bit.ly/39LUF8Y**

OESOPHAGEAL CANCER

Sponge on a string pill

A "sponge on a string" pill test can identify 10 times more people with Barrett's oesophagus than the usual GP route, finds new research.

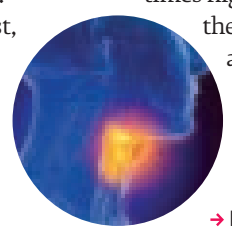
The test, which can be carried out by a nurse in the GP surgery, is also better at picking up abnormal cells and potentially early stage cancer.

Barrett's oesophagus is a condition that can lead to oesophageal cancer in a small number of people. It's usually diagnosed in hospital by endoscopy following a GP referral for longstanding heartburn symptoms.

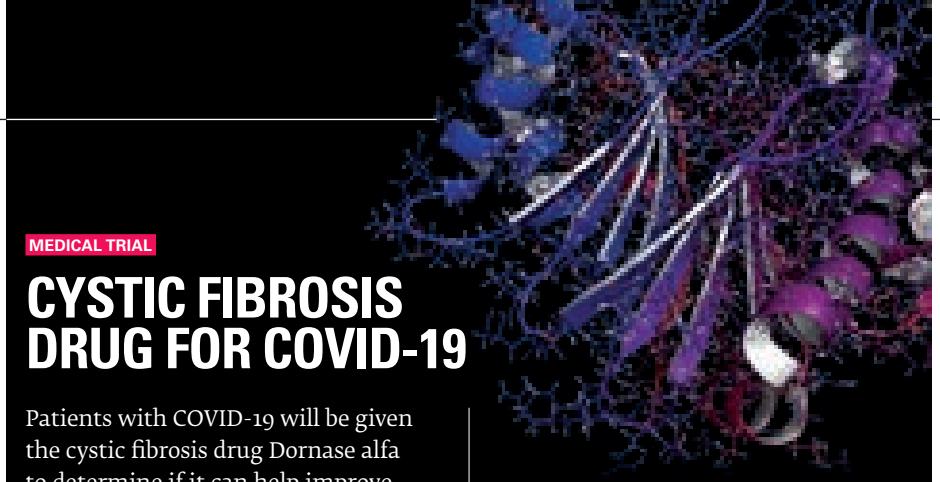
The Cytosponge test, developed by researchers at the University of Cambridge, is a small pill with a thread attached that the patient swallows, which expands into a small sponge when it reaches the stomach. This is quickly pulled back up the throat by a nurse, collecting cells from the oesophagus for analysis using a new laboratory marker called TFF3.

The pill is a quick, simple and well-tolerated test that can help tell doctors who needs an endoscopy.

The researchers studied 13,222 participants. Over the course of a year, the odds of detecting Barrett's were 10 times higher in those offered the Cytosponge, which also led to five early cancer diagnoses, compared with one diagnosis in the usual care group.



→ **bit.ly/30fSXJT**



IMAGES: ISTOCK/SHUTTERSTOCK/SCIENCE PHOTO LIBRARY

MEDICAL TRIAL

CYSTIC FIBROSIS DRUG FOR COVID-19

Patients with COVID-19 will be given the cystic fibrosis drug Dornase alfa to determine if it can help improve survival by reducing excess inflammation in the lungs, as part of a trial co-led by UCL and the Francis Crick Institute.

The COVASE trial has been funded by LifeArc, a medical research charity, and will be run in partnership with University College London Hospitals (UCLH) NHS Foundation Trust. Up to 40 patients are expected to be recruited.

During a viral infection, a group of white blood cells called neutrophils release neutrophil extracellular traps (NETs), which are extracellular meshes whose primary role is to trap and kill bacteria.

Researchers believe the immune system in COVID-19 patients is over-active and an abundance of NETs could be causing excess inflammation (hyperinflammation) and contributing to the onset of pneumonia and severe damage to the lungs.

Select hospital patients will be given Dornase alfa twice a day for seven days and researchers will examine the drug's effect on inflammation and survival. Historic controls will be derived from an existing database of 120 subjects.

→ **bit.ly/319OmYW**

CONSENSUS PAPER

"DON'T DELAY CANCER TREATMENT"

A European Society for Medical Oncology (ESMO) interdisciplinary expert consensus paper on how to manage cancer patients during the COVID-19 pandemic has been published.

It encourages medical oncologists worldwide not to discontinue or delay any type of anti-cancer treatment that may potentially impact on overall survival. The experts also urge an end to labelling all cancer patients as vulnerable to coronavirus infection, since this may lead to inappropriate care and potential negative outcomes.

Earlier this year, ESMO developed guidelines for prioritising the various aspects of cancer care across different tumour types, with the aim to mitigate the negative effects of the pandemic on the management of cancer patients.

→ **bit.ly/2EC1oH3**

COVID TECH NEWS

LGC SERACARE

CE MARK FOR KIT

LGC SeraCare has said the AccuPlex SARS-CoV-2 Reference Material Kit v2 is now CE-marked for *in vitro* diagnostic use (CE-IVD).

With this change in regulatory status, the new product name is AccuPlex SARS-CoV-2 Molecular Controls Kit. Bearing the CE mark and IVD symbol signifies that the AccuPlex SARS-CoV-2 Molecular Controls Kit meets extensive design control requirements.

The technology mimics wild-type pathogenic viruses, but is safe, non-infectious and replication deficient.

→ **seracare.com**

VAPOURTEC

DAILY RISK LIST

Flow chemistry engineering firm Vapourtec has launched a "COVID-19 hotspot tracker" aimed at helping to identify high-risk areas for businesses and individuals as the nation begins to return to normality and local travel increases.

Developed by Vapourtec software engineers, the "league table" encompasses all of the local authorities across England and is updated daily, presenting the latest reported cases of COVID-19 per million of the population.

→ **vapourtec.com**

ROSALIND FRANKLIN INSTITUTE

ENGINEERED LLAMA ANTIBODIES

Researchers have developed a family of engineered nanobodies that neutralise the SARS-CoV-2 virus, targeting the viral spike protein in a novel way.

The team from The Rosalind Franklin Institute, Diamond Light Source, the University of Oxford and Public Health England have hailed the breakthrough as a potential therapy, which could be delivered as part of a combination in a synthetic convalescent serum.

The nanobodies could also be developed as a diagnostic, taking advantage of their very high specificity and affinity.

→ **rfi.ac.uk**

THE BIG QUESTION

THIS MONTH WE ASK

"What are the chances of a COVID-19 vaccine by Christmas?"

Charlie Houston

Chief Biomedical Scientist, Biochemistry
Nobles Hospital, Isle of Man

As of 31/07/20 there are 26 candidate vaccines in clinical evaluation, of which five are in phase 3 clinical trials. There are 139 candidate vaccines in preclinical evaluation.

Various predictor markets – exchanges in which participants buy and sell contracts on future events in fields from politics and entertainment to foreign affairs and science – are indicating there will not be a COVID-19 vaccine this year.

They have put the chance of a vaccine between now and then as less than one in three, or even less than one on five.

Hypermind, which bills itself as a supercollective intelligence, says the best chance – 59% likelihood –is that a vaccine will only be approved sometime after the first quarter of 2021.

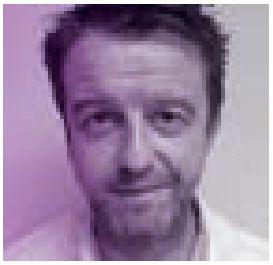
Prediki.com, another online play-money prediction market, is even more pessimistic. It puts the chances of a vaccine being mass-produced before January at one in five.

In fact, the odds of a vaccine only cross 50-50 after June 2021.

A vaccine from the University of Oxford, in the UK, which is under development in partnership with the pharmaceutical company AstraZeneca, states it has obtained "good data so far" on its COVID-19 vaccine candidate and is already in large-scale clinical trials, with results expected sometime in August.

So, the chances we will see an effective and licenced vaccine are low in my opinion. I'd put my money on late April 2021.

IMAGE: ISTOCK



Jonathan M Evans

Lead Biomedical Scientist/ Operational Manager
Virology Specialist Centre, Public Health Wales

Like everybody else, I would love a vaccine to be available by Christmas. Normally, I'd like to think I'd be in a position to give an informed response, but the reality of leading the Wales Specialist Virology Centre response to the COVID pandemic, and helping other labs within the Welsh network come on line, means that my team and I have had very little time to read any of the literature released. I try to avoid getting my scientific updates from the media, for what I believe are good reasons.

However, we have to be realistic and look at both sides. I don't believe a vaccine has ever been made in such a short timescale, I'm not aware of any previous coronavirus vaccines and both SARS and MERS have been around awhile. If developed, you'd have the manufacturing challenges, the logistics of delivery and likely requirement of a cold chain.

On the contrary, there are hundreds of vaccine trials going on globally and money is being invested like nothing I've ever witnessed. I believe humans are incredibly ingenious, clever people who have great problem-solving capabilities when required (or if potentially vast sums of money are involved for the victor).

With Public Health Wales supporting the Oxford University trial and preliminary results looking promising, it would be hugely professionally and personally rewarding if this vaccine was the one!

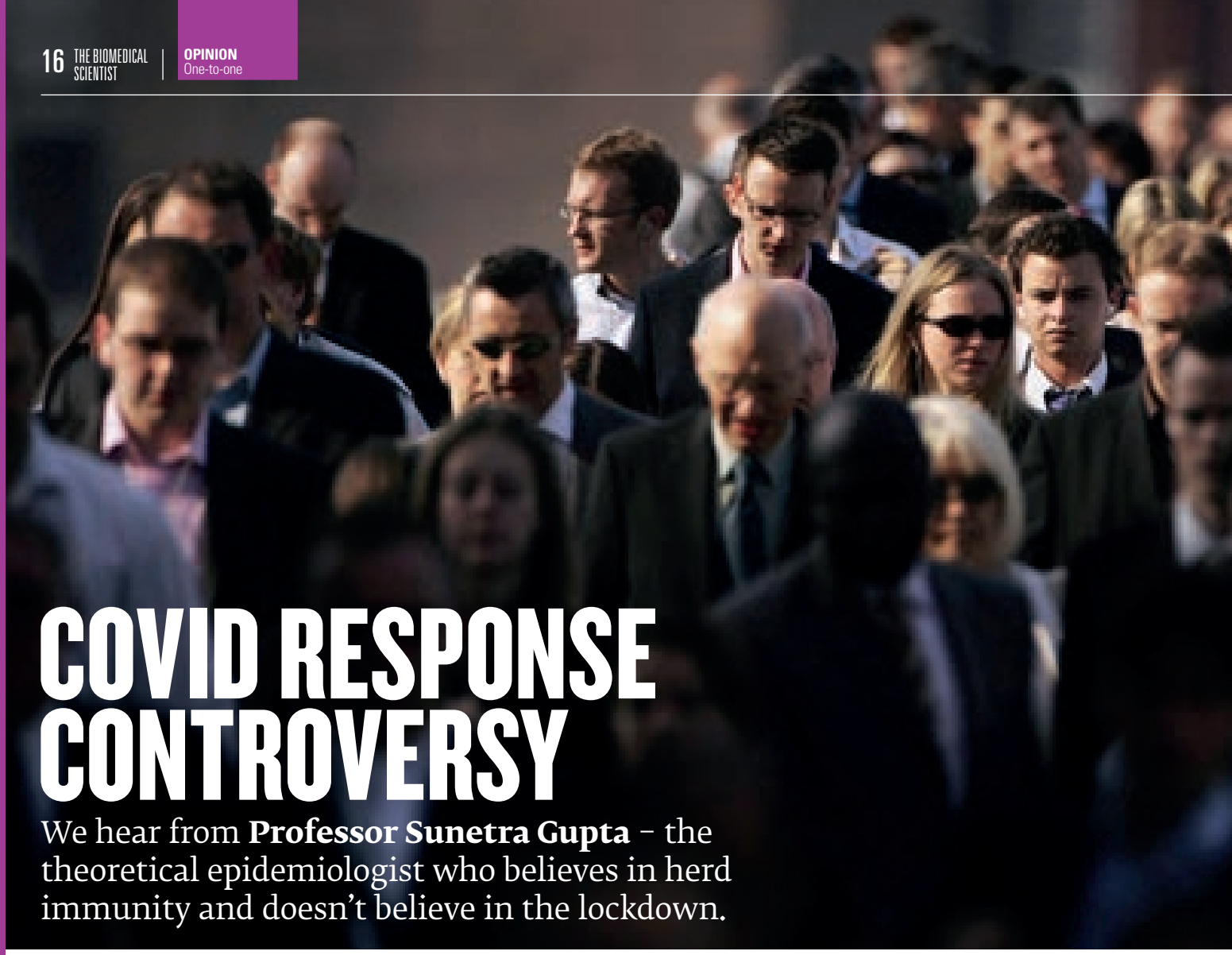
Sarah J Pitt

Principal Lecturer
School of Pharmacy and Biomolecular Sciences, Brighton University

There are a number of candidate vaccines under development around the world and the research teams have taken on a very difficult job, given that we do not fully understand the immune response to coronaviruses in general and that attempts to design a vaccine against the first SARS-CoV and Middle Eastern Respiratory Syndrome virus (MERS-CoV) have not been successful.

The SARS-CoV-2 spike protein S is involved in effecting viral entry into host cells , so finding a way to block that seems important. It is also immunogenic, which is why it has become the focus of vaccine design. A number of approaches are being taken. For example, the Oxford University group have cloned the genetic material for the S protein into an adenovirus vector (ChAdOx1 nCoV-19). The Imperial College team are using self replicating RNA containing the S gene encased in a lipid nanoparticle. Early results from both of these are promising and show that they can stimulate both antibody and T cell responses in humans. The Valneva vaccine, which will be manufactured in Livingstone, is taking the more traditional method of using whole inactivated virus and this might eventually turn out to be a better option.

While there are grounds for cautious optimism, will a vaccine and normal life be possible by Christmas? Only once everyone in the world has been given at least one dose of a safe, effective vaccine. I would be delighted to be proved wrong, but that does seems unlikely.



COVID RESPONSE CONTROVERSY

We hear from **Professor Sunetra Gupta** – the theoretical epidemiologist who believes in herd immunity and doesn't believe in the lockdown.

Professor Sunetra Gupta made the news headlines in March, when she and her colleagues in the Department of Zoology at the University of Oxford ran a predictive model that assumed COVID-19 had arrived in the UK in January – a month earlier than thought. They argued that these extra weeks would have made all the difference, giving the virus enough time to spread to as much as two-thirds of the population, thus achieving a degree of herd immunity. Their research also assumed that only a small proportion of the population, just 0.1%, would be at risk of hospitalisation.

The Oxford model effectively presented a best-case scenario to balance out the worst-case scenario from Imperial College London that had predicted 250,000 to 500,000 deaths in the UK if nothing was done to halt the spread of the disease.

The Imperial model is the one that helped to convince the UK government that a lockdown was the appropriate response to the pandemic.

The Oxford report caused a brief storm, attracting praise and criticism, but was soon lost among the many other COVID storms. But Professor Gupta was back in the news in June, arguing that we ought to have come out of lockdown much sooner – for her, the economic damage being wrought, especially to disadvantaged sections of society, was greater than the impact of the virus.

Looking back on these events from the distance of a few more months, Gupta is standing firmly by her work and her words. "We were not saying that is what had happened, but that it was a possibility. We were laying out a scenario that fitted the data at that point. One scenario, which the Imperial College team had outlined, was that the virus had arrived very recently, had not spread much to the population and had killed a substantial fraction of those infected. And what we were trying to say was equally compatible with the data is this scenario where it arrived earlier."

Now all the barriers have been removed, it is increasing. I don't see any surprises in that pattern

A resurgence?

Nothing she has seen since, not even a seeming resurgence of cases, has caused

her to reevaluate the scenario. "I don't think we are seeing a resurgence," she says. "It's a useful piece of information to know that lockdown worked in certain areas, to slow down the virus and to stop it from spreading from, say, a town to a village. But as soon as you lift lockdown, the virus comes back."

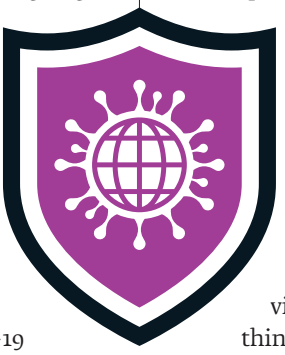
So the natural spread of the virus has merely been delayed? "It's not really a resurgence. It's just where it didn't increase in the first place. Now all the barriers have been removed, it is increasing. I don't see any surprises in that pattern. What I do think is interesting is that it's not resurgent in many areas that did suffer the full brunt of the pandemic, so in London, New York, northern Italy, Sweden." For Gupta, this implies that in these areas levels of herd immunity may have been reached, meaning the spread of the virus is now being contained. The key step now, she says, is to use serological testing to determine what proportion of the population has been exposed to COVID-19.

Another factor that interests Gupta is the extent of cross-immunity from exposure to other coronaviruses. "I thought it might protect only against disease, but we've learned that these cross-immunity responses can actually protect against infection. That makes it hard to use antibody tests to get a measure of how many people have been exposed to the virus. But the good news is that if a fraction of the population is already resistant to infection, that brings the threshold for herd immunity down substantially."

Economic vulnerability

If herd immunity is permitted to build, the question of the vulnerable sections of the population becomes even more pressing. "I think the best strategy for protecting the vulnerable is to shield. Obviously mistakes were made in terms of sending infected people back to care homes. I think we should be very careful, especially when we move back into winter. But in many parts of the UK, the infection rates are down to a point where people can make a sensible decision about what level of risk to take."

She is still no fan of lockdown, even the eased version. "I don't see any clear and rational thought behind it. More importantly, my primary reason for being vocal has all along been my deep concern about the economically vulnerable, in this country and globally. I am terrified when I read reports of 260 million people going under the poverty line as a result of these measures. We also have to think of the young and what they have been denied."



Consider all consequences

What then, for her, are the key scientific lessons to be learned so far from the COVID-19 response? "It's important to put every bit of effort into understanding how the immune response to the virus affects infection, disease, and severe disease. That's not a huge revelation, but what I hadn't anticipated was that the cross-protection from other coronaviruses goes much further than expected. Serological surveys are also critical. We've been looking at blood banks in Scotland and can see infections going up in mid March, which suggest the virus was there in February. Then there's the work in the sewers where they're looking for the virus. I think it's important to have these sentinels in place to try and see when the virus arrived and where it spread."

There are also political lessons: "I think it's important not to look at the situation along the one dimension of 'how are we going to get this under control?' We must consider all the consequences. I think we also need to take a more holistic view and not just this individual, nationalistic view. Think globally, think internationally." BMS

SUNETRA GUPTA

- ✔ Professor of Theoretical Epidemiology at the Department of Zoology, University of Oxford
- ✔ **1987** – graduated from Princeton University
- ✔ **1992** – PhD, Imperial College London
- ✔ **2009** – winner of the Royal Society Rosalind Franklin Award for her scientific achievements
- ✔ Author of five fictional novels

IMAGES: GETTY

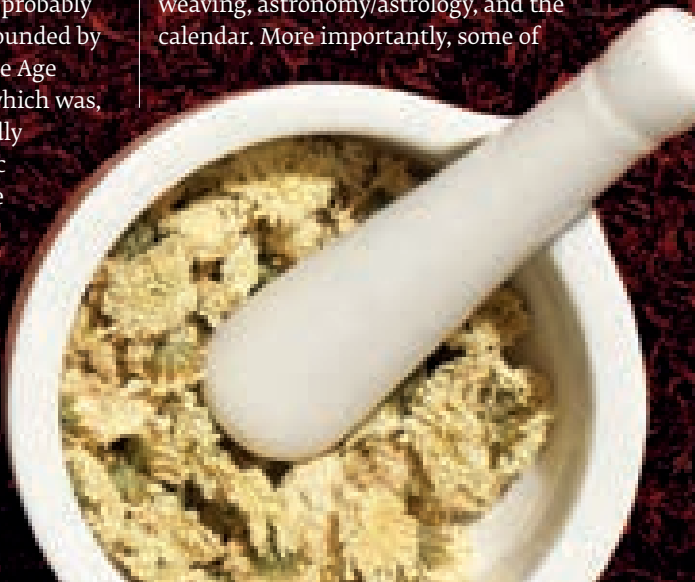
Stephen Mortlock looks back over the medical history of one of the most ancient civilisations on earth.

CHINESE MEDICINE

FROM THE SHANG DYNASTY TO THE CURRENT PANDEMIC

The discovery of the *Shu Ape* – a mouse-sized primate (weighing only 100 to 150 grams) from the Middle Eocene Epoch (4.5 to 4 million years ago) appeared to support the Chinese "regional evolution" theory of an independent basis for the origin of man, in contrast to the theory that all human beings originated in Africa. Certainly, excavations have shown evidence of cultivated rice being grown at Neolithic sites along both the Yellow and Yangtze rivers around 10,000 BC. At Damaidi (a small village in the Weining Mountains on the Yellow River), cliff carvings dating from 6000–5000 BC have been discovered showing scenes of the sun and moon, celestial bodies and people hunting, herding and grazing animals. Neolithic culture was characterised by a settled lifestyle, based on farming and the rearing of domesticated animals, while the use of more sophisticated tools led directly to a growth in crafts, such as pottery and weaving. Archaeologists have shown that ancient Chinese potters produced delicate, polished and coloured vessels used for both functional and ceremonial purposes.

The Chinese Imperial reigns probably started with the Xia dynasty, founded by Yu the Great in the early Bronze Age (between 2070 and 1600 BC), which was, until the late 1950s, a supposedly mythical dynasty, but scientific excavations found early Bronze Age sites including palace buildings and bronze smelting workshops at Erlitou on the Yi River. Evidence also suggests that there were several other clans living alongside the Yellow River at this time. Dynasties rise and fall and the Xia dynasty was eventually overthrown by the Shang dynasty (from 1600 to 1046 BC), another clan found along the Yellow River valley. It was then that the earliest pieces of writing (on pieces of tortoise shells and bone) start to appear and these show the development of agriculture, the brewing of alcohol, silk weaving, astronomy/astrology, and the calendar. More importantly, some of



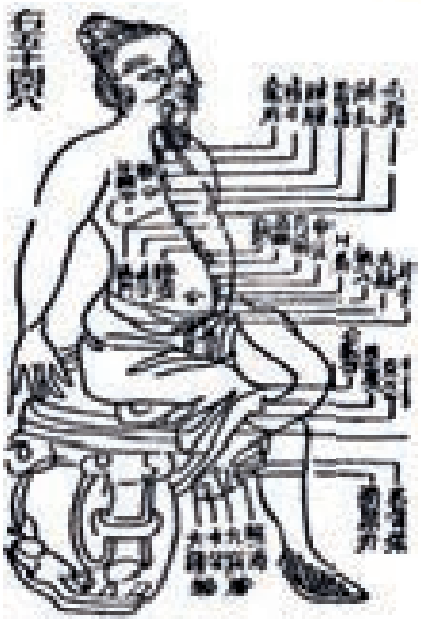
PHOTOGRAPHY: RICHARD GLEED

these writings also have references to headaches, eye ailments, abdominal ailments, parasites and other illnesses.

From the year 1046 BC, Chinese culture flourished under the reign of the Zhou Dynasty and their influence spread across China. The greatest and best known Chinese philosophers and poets – Confucius, Mencius, Mo Ti (Mot Zu), Lao-Tzu, Tao Chien, and the military strategist Sun-Tzu – all came from this time and many philosophical schools were founded, which are referred to collectively as the "Hundred Schools of Thought" interestingly, around the same time as Greek philosophy was emerging and the four most influential schools (Confucianism, Taoism, Mohism and Legalism) were established.

Chinese medicine

As with many other cultures, Chinese medical activities probably began long before there were written languages or records. Archeological material proves that the roots of China's written language may extend back some seven thousand years, but the first evidence comes from the Shang dynasty. The Shang people were religious and it was believed illness resulted from upsetting an ancestor, being cursed or an evil demon entering the body and being cursed. So often cures involved placating ancestors with suitable rituals or asking their help to expel the demon. People turned to "Shamans", mediators skilled in talking to the ancestors, who in turn talked to Shang Ti (their deity) for advice. Questions written on "oracle bones", usually scapula bones or tortoise shells, which were heated and the cracks were "divined", in other words, read by the shaman to find an answer. Much was actually recorded during this period, incorporating the different philosophical ideas. The major medical classic, the *Huang Ti Nei Ching (Yellow Emperor's Classic of Internal Medicine)* was written down to consolidate ancient medical experience and theory into one compendium. It detailed the body's anatomy and functions, the blood and circulation, physiology, pathology, diagnosis and treatment, acupuncture and moxibustion (a form of heat therapy in which dried plant materials called "moxa" are burned on or very near the skin) and the use of ethnopharmacology (herbal medicine). These ancient writings describe a medical theory that focused on the circular movement of qi (氣, qì, pronounced "chee", air or vapour) and xuè (血, "shui", blood). Ill health was understood as a stagnation, or deficiency preventing the proper movement of qì or xuè, which would result in an imbalance of yīn (陰) and yáng (陽). Physicians demonstrated that the human body was an organic whole, and that its health and illness was intimately connected to the natural environment, including the five elements (wood, fire, earth, metal, and water). This text made a vast and profound impact on successive generations of medical practitioners and scholars, and has continually guided Chinese medicine's clinical application. There are also texts showing that these early doctors were evaluated and tested by more experienced doctors to ensure they attained certain levels of competency.

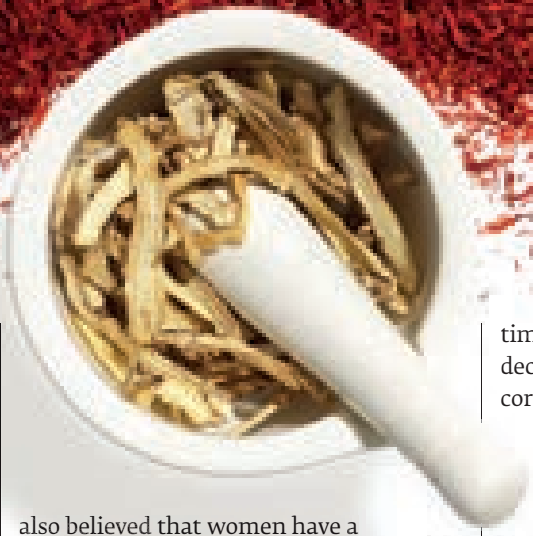


From the year 1046 BC, Chinese culture flourished under the reign of the Zhou Dynasty

The Zhou dynasty

During the Western Zhou dynasty, imperial doctors were divided into four departments: dietetic, diseases, sores and veterinary. They had a wide range of proven remedies and the number of commonly used medicinal materials exceeded a hundred, consisting of herbs, animal material, and minerals. These historical facts are recorded in the Zhou dynasty's system of standards, *Zhou Dynasty Rites*, the first ancient compilation of verse, *The Classic of Poems*, and *The Mountain Sea Classic*. In the Zhou dynasty, the dietetic physician was elevated to a very high position and dietetic therapy had a huge impact on following generations. Historically, all Chinese medical experts expounded on this aspect of therapeutic treatment, and Chinese *Materia Medica* contain many kinds of fruits, vegetables, grains, and meats. Today, specialised dietetic texts dating from the Tang dynasty, entitled Medicine Amidst Food and Culinary Therapies, are still published in China.

Medical scientists, such as Zhang



Zhongjing (150 to 219 AD) wrote numerous volumes detailing work on epidemics, external heat disorders, jaundice, and gynaecology, eventually producing a complete set of treatment principals. Hua Tuo (110 to 208 AD), invented an anesthetic called *"Mafei San"*, which was basically powdered cannabis, taken orally, which caused the patient to lose consciousness, making it possible to perform elaborate surgery. During the third century AD, the medical specialist Wang Shuhe organised the theories of pulse reading into China's first comprehensive work on pulse reading. It summarises the pulses into 24 types, and expounds on the relationship between the pulse, physiology, and pathology. This systematised the theory and method of pulse reading – one of the outstanding achievements of Chinese medicine.

The Tang dynasty

Sun Simiao (540 to 682 AD), the Tang dynasty medical scientist, researched and understood each aspect of Chinese medicine, including physiology, pathology, diagnosis, treatment, herbs, prescriptions, and other essential theory, as well as internal medicine, external medicine, gynaecology, paediatrics, acupuncture, massage, Qigong, alchemy, and dietetics. His body of work is extensive with a supplement on herbal medicine that gives instructions for the correct time to harvest and process over two hundred types of herbs. This text elaborates on the fact that differing quality of soil, water composition, and climates can affect the same herbs from different areas, causing a variation in quality. He wrote "If you do not know the proper seasons when they should be placed in the shade or in the sun to dry, the result will be that you know their names but do not obtain their intended effects. If you gather them at an improper time, they will be good for nothing." He also believed that women have a special physiology, and that during menstruation, pregnancy and childbirth they are more susceptible to illness. Sun said "the reason there are separate prescriptions for women is that they get pregnant, give birth, and suffer from uterine damage. This is why women's disorders are ten times more difficult to cure than those of males." He wrote a text with prescriptions and treatments specifically for women and children.

The Song dynasty

The invention of the printing press and further advances in paper-making allowed large quantities of Chinese medical texts to be printed. This caused Chinese medicine to spread, giving rise to widespread, deep research. Specialisation in Chinese medicine continued to develop and experts emerged. Many different schools of thought, with different academic arguments, came into existence and brought about many new viewpoints. In 1247, during the Song dynasty, Song Ci (1186 to 1249) published his book *Collected Cases of Injustice Rectified*, which recorded human anatomy, coronary methods, emergency treatment, detoxification, and other information. What is interesting is a section titled "Difficult Cases". This text is a fairly early work on forensic medicine and explains how to use evidence to determine cause of death in unusual cases, especially if the death is suspicious or possibly an intentional death made to look accidental. And he was able to determine the time of death by the rate of decomposition or show whether the corpse had been moved. Song Ci also compiled a pharmacopoeia of useful herbs that could be used to make obscure injuries appear.

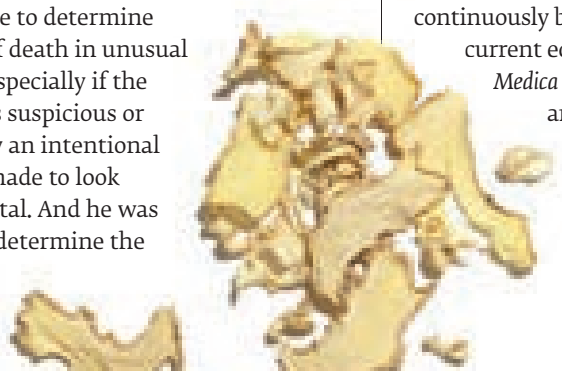
Herbal Medicine

Around 6000 years ago, a Chinese farmer called Shennong taught people how to cultivate grains as food and it is said he tasted hundreds of herbs to carefully test and record their therapeutic properties. *The Divine Farmer's Materia Medica* (or *Shennong Ben Cao*), first compiled around 206 BC, is considered to be the earliest Chinese pharmacopoeia, with over 360 herbs that he had classified into three groups. The first group are food herbs that are eaten for health maintenance, longevity and illness prevention. The other two groups are called medicinal herbs that are dispensed to each patient as an individual formula based on one's unique constitution, environment, and medical condition.

The Chinese Materia Medica

From 206 BC to the late 16th century, many more herbs were added to what became known as the *Chinese Materia Medica*, the book of Chinese herbal medicines. This increased the total to 1892 distinct herbs and more than 10,000 formulas. Over several millennia, many Chinese physicians made new discoveries, theories, and classifications, often writing or compiling books that have become classics of Chinese medical literature and are still referenced today. New entries are continuously being added and the current edition of *Chinese Materia Medica* contains over 10,000 herbs and natural substances.

Liquorice, often called the "grandfather of herbs" is used in the majority of prescriptions



to balance out the other herbs and "improve" the flavour. But, people have chewed liquorice roots for oral hygiene for as long as the plant has existed. It is well known for its detoxification powers, reducing the toxicity of nicotine and caffeine. It has anti-inflammatory and anti-allergy properties, helps with digestion and eases respiratory problems. The bright yellow turmeric powder is used in curries from all over the world and has been used as an alternative to saffron in paellas and other saffron-based dishes. Its use in medieval Europe led to it being nicknamed "Indian Saffron". In Chinese herbal medicine turmeric did not appear until the Tang dynasty (7th century), a time of great international trade and was probably imported to China from India. Turmeric comes from the root of the *Curcuma longa* plant, and has a tough brown skin and a deep orange flesh. This herb has a peppery flavour, both warm and bitter, while its fragrance is mild. The active constituent in turmeric is called curcuma. Turmeric plants belong to the category of herbs that invigorate the blood. As the name indicates, these herbs tend to stimulate the blood flow and are used to help the circulation of blood in cardiovascular conditions or menstrual irregularities as well as to treat acute pains caused by blood stagnation. It was also used to relieve congestion and resolve bruising and clots, aid digestion, dissolve gallstones and decongest the liver. Not to forget being used for nosebleeds and heatstroke.

Turmeric has similar effects to steroidal and non-steroidal anti-inflammatory drugs in reducing swelling and pain, but without the side effects or risks of the drugs. Due to these properties, it is used in Chinese medicine for rheumatic conditions, especially for the shoulder. More recently, there has been a lot of research into the cancer-fighting properties of turmeric. Studies have claimed frequent use of turmeric is linked to lower rates of breast, prostate, lung, pancreatic, oral and colon cancer.

Ginkgo biloba

Ginkgo biloba was all the rage a couple of years ago and powders and pills started appearing in health food shops and can even be found in supermarkets these days. *Ginkgo biloba* L. of the Ginkgoaceae family is a deciduous tree (20–40 metres height) native to eastern China and is considered a "living fossil" since it is thought to have originated 200 million years ago. It was first recorded as a medicinal plant in the *Chinese Materia Medica Shen Nong Ben Cao Jing* approximately 2,000 years ago, and only the seeds were reported to be used as medicine. Much later, the leaves of *G. biloba* were cited for the treatment of heart and lung diseases. The nuts were chewed by monks when they had to sit for hours in meditation, as it reduced urination; recent studies have shown that *G. biloba* extract 761 can alter the volume of urine excretion. The nuts are edible, when cooked, and can be used in a variety of Asian dishes, one of the more famous being "Buddha's Delight", which is one of the many dishes eaten during the Chinese New Year celebrations. *G. biloba* has a bitter-sweet, astringent property, is associated with the lungs and can be used for asthma, coughs and chronic inflammation from allergies. It is also used for cardiovascular conditions, stomach upsets and eye conditions. It has long been used to treat erectile dysfunction in China and is an ingredient in modern-day Viagra. It has been claimed that it can be used as a cure for bad memory; its abilities to slow mental decline and as an overall tonic for the mind have been documented. On the downside, some people find they are allergic to the outer fleshy part of the nut and skin reactions – such as blisters or itchy irritation – can occur if gloves are not used when handling the fruit.

The invention of the printing press allowed large quantities of Chinese medical texts to be printed

Flavones

Georgi root (*Scutellaria baicalensis*) or Chinese skullcap is the traditional Chinese herb Huang-qin. It is a member of the mint family (Lamiaceae) found in sandy mountain soils in northeast China and adjacent Russia, Korea, Mongolia, Japan, and the mountains of southwest China, north of the Yangtze River. It is probably the most widely used of the 98 species of *Scutellaria* that occur in China. It was first described in Western terms by a German-born botanist Johann Gottlieb Georgi (1729–1802), a professor of the Russian Academy of Sciences in St Petersburg. Its first mention in Chinese *Materia Medica* (herbals) comes in *Shen Nong Ben Cao Jing* in the middle class of drugs. It has been applied in the treatment of diarrhoea, dysentery,

hypertension, haemorrhaging, insomnia, inflammation and respiratory infections. Flavones, such as baicalin and wogonoside, and their aglycones, baicalein and wogonin, are the major bioactive compounds extracted from the root of *S. baicalensis*. These flavones have been reported to have various pharmacological functions, including anti-cancer, hepatoprotection, antibacterial and antiviral, antioxidant, anticonvulsant and neuroprotective effects. Lung Fufang, a traditional prescription using Huang-Qin, can prolong the survival rate of patients with primary bronchial pulmonary squamous cell carcinoma, and it has a similar effect on NSCLC (non-small-cell lung cancer) patients. Huang-Qin is also a major ingredient of Fuzheng anti-cancer prescription, which when used in combination with chemotherapy is shown to have improved outcomes on NSCLC in middle- and late-stage patients, compared with chemotherapy alone.

Recent developments

Famously, the gold-standard malaria drug, artemisinin, was discovered in China — isolated from sweet wormwood *(Artemisia annua)*. *Artemisia annua*, known as *qinghao,* is celebrated in traditional Chinese medicine as a treatment for malaria. However, early medicinal records also show it to be a remedy for haemorrhoids and used as an anti-inflammatory.

More recently, artemisinin and its derivative artesunate have shown a potential to stop viruses reproducing, including CMV, HSV-1 and HCV. A study conducted in China in 2005 also found that compounds extracted from four herbs, including *Artemesia annua*, showed moderate antiviral activity in laboratory cells against the original SARS virus, which is of course closely related to the current coronavirus.

This involves the four pillars of diagnosis – looking, listening, touching and asking

Conclusions

Over thousands of years traditional Chinese medicine has developed a theoretical and practical approach to the treatment and prevention of disease. The first documented source of Chinese medical theory, the *Huangdi Nei Jing* (*"Inner Classic of the Yellow Emperor"*) was written between 300 BC and 100 BC. It describes the diagnosis and treatment of a huge range of disorders and gives advice about healthy lifestyles, exercise, and dietary advice to avoid micronutrient deficiency diseases such as beri-beri, xerophthalmia, and goitre, which conforms remarkably well with current recommendations for the prevention of chronic disease. Chinese medicine developed and was passed on from a very early time; the result is a legacy of works exceeding 8000 texts dealing with every sort of health problem, including the common cold, venereal disease, paralysis, and epilepsy. This knowledge is contained in books and manuscripts bearing such enigmatic titles as *The Pulse Classic* (compiled by Wang Shuhe in the 3rd century) and *Prescriptions Worth a Thousand Pieces of Gold* (by Sun Simiao in the 7th century).

As we compare the treatments from traditional West and East, both are associated with the imagination of the human body and medicinal materials. Before orthodox medicine revealed the real cause of disease, human beings had a long history of creative imagination about the inner and outer self. While ancient Chinese perceived the body in an adequate balance characterized by Yin and Yang, medieval European doctors invoked the hot/cold dichotomy but the principles of treatments are surprisingly the same. In one medieval medical book, *Causae et Curae* written by Hildegard of Bingen (1098-1179), there are treatments very similar in both European and Chinese medicine – vinegar or equivalent was used as a warming treatment "to warm the stomach and bladder". As with most forms of traditional medicine, the theoretical and diagnostic basis of traditional Chinese medicine cannot often be explained in terms of Western anatomy and physiology. It is rooted in the philosophy, logic, and beliefs of a different civilization and leads to a perception of health and disease. Whereas a doctor of traditional Western medicine might be interested in body weight, height and symptoms during an examination, the Chinese medicine doctor looks at a patient holistically. This process involves the four pillars of diagnosis – looking, listening, touching and asking, which can provide important indicators as to the balance, harmony, and energy of the patient. They can then provide the necessary treatment, and two patients with the same symptoms might be treated very differently. Which method is better? The answer is "both", or "neither". We should try and integrate both into a universal approach to healing and treatment, then perhaps we will all be a little healthier and wiser. BMS

Stephen Mortlock is Pathology Manager at the Nuffield Health Guildford Hospital.
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LABORATORY ERRORS IN TRANSFUSION

Anne Lockhart, IBMS representative on the Serious Hazards of Transfusion (SHOT) steering group, explains the latest annual report.

SHOT is the United Kingdom's independent, professionally led haemovigilance scheme. Since 1996, SHOT has collected and analysed anonymised information reported in the UK about serious adverse reactions and other serious adverse events related to blood transfusion. The annual SHOT report for incidents reported in 2019 has now been published. Haemovigilance reporting in the UK continues to increase year on year, with a total of 4248 reports being received.

In 2019, 2.3 million blood components were issued in the UK. Transfusion in the UK is generally safe, with the risk of serious harm being one in 17,884 and death one in 135,705 transfused components in the UK. Non-infectious complications, especially operational procedural errors and those related to transfusion decisions, continue to be the most common causes of transfusion-related deaths in the UK. Delays in transfusion and pulmonary complications (mainly transfusion-associated circulatory overload (TACO)) were the main causes of reported transfusion-related deaths in 2019.

Laboratory errors

Laboratory errors occurred at different stages of the transfusion process. In 2019, the number of events raised to SHOT by the laboratory accounted for 796/3397 (23.4%) of all accepted reports, which is a reduction in the reports submitted in 2018 (885/3326 (26.6%)).

Nearly half of the reports submitted (373/796) were related to component labelling, availability and handling and storage errors. The number of handling and storage error (HSE) reports has almost doubled from 69/530 (13.0%) in 2018 to 107/495 (21.6%) in 2019. The highest proportion of errors occur within the IBCT-specific requirements not met (SRNM) category, with testing errors within this category showing a marked increase from 45/114 (39.5%) in 2018 to 80/157 (51.0%) in 2019. It is apparent from the errors being reported that previous SHOT recommendations do not seem to have been embedded within laboratory culture.

Laboratory errors contributed to three ABO incompatible (ABOi) transfusions in 2019 (considered a never event). All cases were due to component selection errors. Two of these errors occurred during a major haemorrhage situation.

Three key SHOT messages have been created from analysing the laboratory errors in 2019:

"Transfusion in the UK is generally safe, with the risk of serious harm being one in 17,884"

- Many mistakes may be the result of distorted decision making or cognitive bias. Processes should be designed to account for these biases by drawing attention to safety critical steps
- Regular monitoring of quality system outputs is required. If omissions or inaccuracies are detected these require immediate corrective and preventative action (CAPA) to prevent potential patient harm
- Laboratory staff should be comfortable working within routine procedures – these procedures should be safe and fit for use, especially in high-pressure situations.

Deaths and major morbidities

In 2019, there were 15 deaths reported, though none were directly related to blood transfusion (imputability score of 0, excluded or unlikely). Two further cases were reported with major morbidity. One case included sensitisation to the K antigen, and the other was due to delays in the major haemorrhage setting (imputability 1, possible). There were also eight cases reported where minor/moderate morbidity occurred.

IT errors

IT has become integral to the day-to-day working in the transfusion laboratory; there is always further scope to improve the functionality and interoperability of IT within the hospital to increase the safety of these systems. SHOT data continue to highlight that many IT errors are caused by multiple warning alerts, contributing to staff experiencing alert fatigue. A structured, proactive approach is suggested to address this issue including regular review to reduce alerts and making all alerts actionable.

Training and competence

Thorough training and competency assessment of staff is essential to prevent errors. However, for this to occur

competency assessments need to be fit for purpose. Incidents do still occur despite staff being deemed competent in a process, highlighting that training and competence must include the non-technical aspects of the process along with the technical components. Robust and effective competency assessment requires "UPTAKE" of a collaborative assessment process between management and staff members:

- **U**nderstands procedure being assessed
- **P**erforms task accurately
- **T**akes heed of limits of procedure
- **A**pplies knowledge of scientific background and rationale for procedure
- **K**nows and considers risks of not following process
- **E**xplains exceptions and where to find further advice if needed

A key recommendation is that clinical and laboratory staff should be trained in the fundamentals of transfusion, human factors, cognitive biases, investigating incidents and patient safety.

Lab recommendations

- **Knowledge and skills.** Laboratory staff should have knowledge of the clinical requirements of transfusion to work collaboratively to deliver cohesive patient-centred care
- **Knowledge and skills.** All lone workers should be adequately supported through their training and competency assessment to ensure they are equipped with adequate skills and knowledge.

"When errors occur, it is essential that investigations look beyond the staff involved"

Laboratory management have a responsibility to ensure all staff members are competent before exposing them to lone working

- **Knowledge and skills.** Escalation procedures for lone workers must be clear and defined, with specialist support being accessible at all times
- **Information technology.** Laboratory information management systems (LIMS) should be robust and used to their full functionality, preventing ABOi units being assigned to the patient record, and thus issued, especially in an emergency when the patient's blood group is unknown

Key learning points

Training and development

- A robust competency assessment must be completed prior to performing laboratory tasks. Always raise concerns if unsure of a process

Information technology

- Laboratory and quality management should review their LIMS to ensure specific requirements are visible at all key points of the transfusion process. They should work with LIMS providers to rectify any issues uncovered

Knowledge and skills

- Laboratory staff should stop and objectively review all component labelling prior to release to the clinical area. Never assume and always check previous steps have been performed correctly
- Staff booking in samples must follow good manufacturing practice (GMP) working and must not be distracted

When laboratory errors occur, it is essential that investigations look beyond the staff involved as being the only reason for the error. Errors attributable to "human factors" persist, and so systems and practices must be re-assessed, and re-designed to minimise the effect of human error. Policies and procedures need to be as simple as possible, whilst still containing all relevant technical information, to ensure that staff have access to concise instructions and information at all times. Furthermore, laboratory processes should be reviewed to determine that they are robust enough to address current challenges and guidelines and are designed around human factors.

The standard of transfusion knowledge and education within laboratories is becoming a prevalent source of error. The UKTLC is due to release updated guidance around the minimum standard of training and education expected for staff working in transfusion laboratories to address these concerns. All staff should be trained in the fundamentals of transfusion, human factors, cognitive biases, investigating incidents and patient safety principles. Using a holistic approach such as this will ensure that the transfusion process is centred around safe, high-quality, patient-centred care. It also embeds a strong culture of organisational learning from any incidents that may have occurred.

In conclusion, it is recognised that pathology services continue to be under intense pressure in a climate where the workforce is stretched and under-staffed. It is even more vital that staff remain vigilant at all steps of the transfusion process and that duty of care is upheld to ensure safe transfusion and patient safety. BMS

Anne Lockhart, from the Scottish National Blood Transfusion Service, is a Specialist Advisory Panel Representative (Transfusion).

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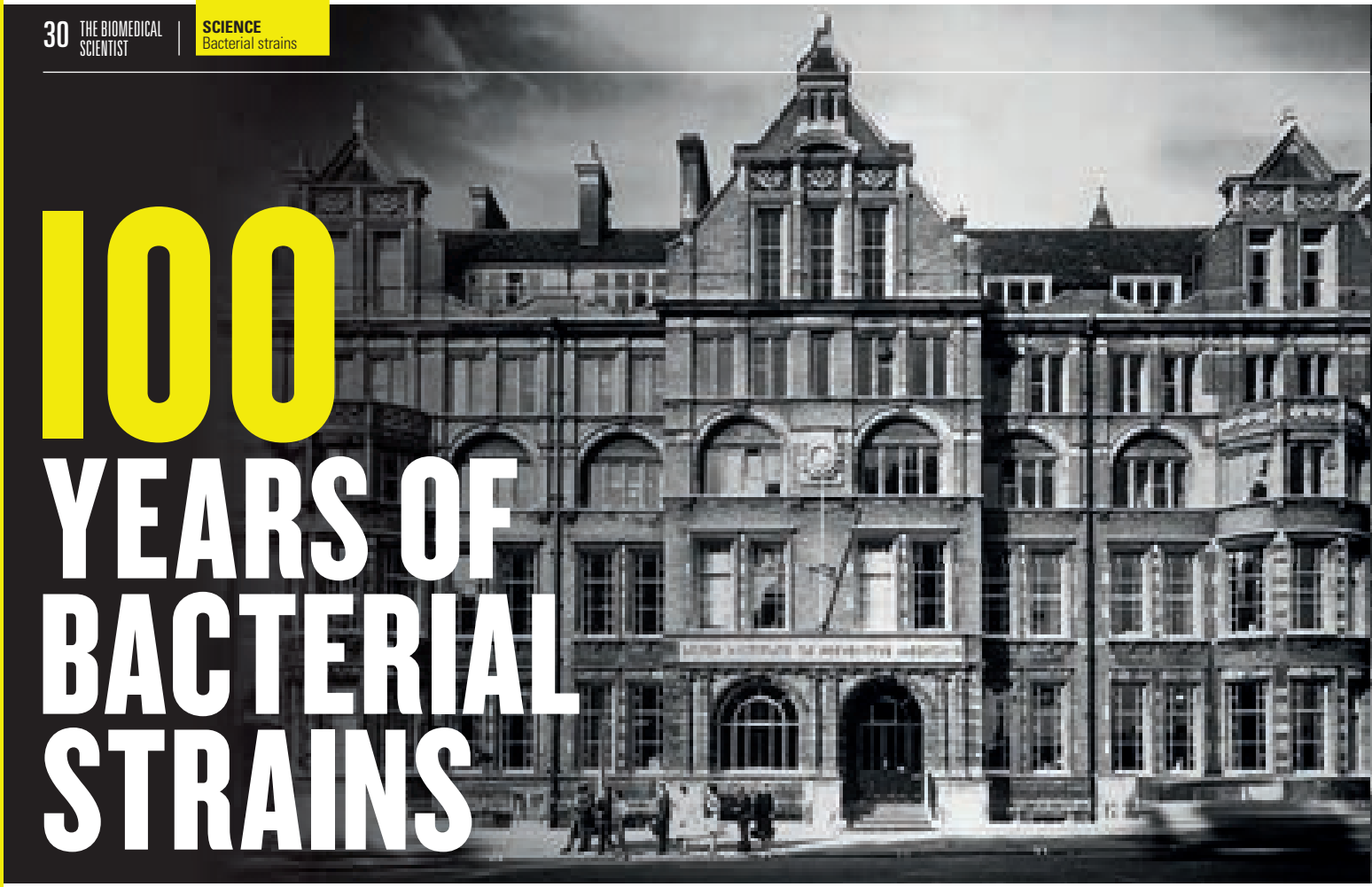

100 YEARS OF BACTERIAL STRAINS

Sarah Alexander and **Ayuen Lual** from the National Collection of Type Cultures look back over a century of providing authentic bacterial strains.

The National Collection of Type Cultures (NCTC) is a bacterial strain collection that exists to serve the ever-changing needs of the clinical microbiology community. Founded in 1920, the collection was established by the Medical Research Council (MRC) under the directorship of Dr Ledingham, Chief Bacteriologist at the Lister Institute, who recognised there was a specific requirement for a "reputable establishment to provide a source of authenticated bacterial strains from a trustworthy source". To date, one century on, the NCTC has seen many changes including a world war, six relocations and eight different curators, but its remits remain largely unchanged. Operated by Public Health England and located over two of its flagship microbiology sites (Colindale and Porton Down), the NCTC is the oldest bacterial strain collection in the world, which was specifically established to provide scientists with bacterial strains. In its 100th year it is still thriving.

The collection currently houses over 6000 different bacterial strains made up of over 900 different species from 82 bacterial families. Whilst the NCTC is taxonomically very diverse, what all strains within the catalogue have in common is that they are of clinical significance, with many (but by no means all) being human pathogens from the Advisory Committee for Dangerous Pathogens (ACDP) hazard groups 2 and 3.

The early years

The NCTC has strains in the catalogue that are older than the collection itself. The nucleus of the original NCTC collection was created from a private collection of 100-200 strains that were already in existence within the Lister Institute and were being provided to scientists on an *ad hoc* basis. These were largely a collection of Enterobacteriaceae strains curated by the then prominent scientist Sir Fredrick Andrews, who had a strong research interest in *Shigella* strains. Dr St John-Brooks was appointed as the first curator of the NCTC and under his leadership the collection expanded quickly, with nearly 100,000 cultures

OVER THE PAST 100 YEARS, THE NCTC HAS SEEN:

1
World war

6
relocations

8
curators

being dispatched to scientists between 1920-1940. During this period the collection had grown to over 800 strains, which were preserved on bacteriological slopes that were sealed with parafilm.

In 1935, early experiments were conducted into bacterial freeze-drying – a process that employs a low temperature dehydration process, firstly freezing the product then reducing the pressure, which removes any ice by sublimation. This is now regarded as the gold standard of bacterial preservation for the vast majority of bacterial families and the NCTC was a very early adopter of such technology.

In 1939 the master banks of every strain within the NCTC catalogue were freeze-dried in duplicate. By 1949 freeze-drying was a routine procedure in the NCTC with all strains being preserved and shipped to customers in this format. Indeed, this technology has remained largely unchanged and in 2020, the NCTC centenary year, all strains within the collection are freeze-dried. Whilst this has a number of benefits, including reduced transportation costs as strains can be shipped at ambient temperature, and strain preservation as this technique minimises the necessity for sub-culture, not all bacterial species can be preserved using this method. Until recently only strains that were robust enough to endure this method of preservation were accepted into the collection. However, such a rigid acceptance criterion has excluded some very significant bacterial pathogenic families which, whilst being impressive stealth pathogens, are too fragile to survive the lyophilisation process. Within the last year the NCTC has invested resources into ensuring that more fastidious strains, which cannot be preserved using desiccation techniques, such as *Chlamydia trachomatis* are accepted into the catalogue. It is anticipated that in 2021 obligate intracellular pathogens and other more fastidious strains will be available from the NCTC.

Type strains

The NCTC, like other bacterial culture collections around the world, has a specific remit to support scientists involved in bacterial taxonomy who wish to describe novel bacterial species. In 2019 the NCTC accepted over 200 new bacterial strains into the collection with the specific remit from the depositors to supply these strains to any bacteriologists who wish to use them for scientific research. A quarter of these new accessions to the catalogue were type strains, with each one presenting a newly described bacterial species. The designation of a "type strain" is unique to prokaryotic taxomy and an essential part of the process in describing a new bacterial species. If a scientist, for example, was to describe a new animal species it would not be necessary to provide a biological exemplar and deposit it within an international repository where other scientist could access said material to confirm scientific reproducibility. However, the International Code of Nomenclature of Prokaryotes (ICNP), which governs the naming of bacterial species, dictates that

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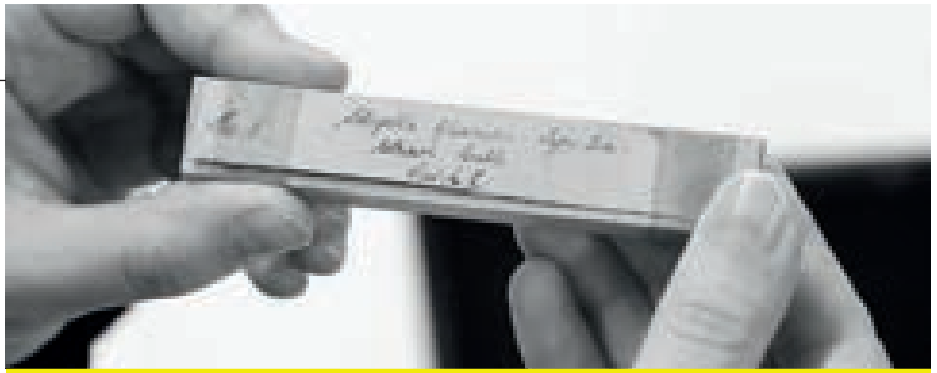

in order to propose a new bacterial species the scientist must deposit a biological representative (designated the "type strain") into two different recognised bacterial repositories and the work describing their unique features to justify its species status must either be published in the *International Journal of Systematic and Evolutionary Microbiology (IJSEM)* or another equivalent publication that is published within the IJSEM official lists. Having to define and accession a bacterial type strain into a bacterial repository prior to publishing and describing the species ensures that bacterial taxonomy is accountable to scrutiny and ultimately is reproducible.

Control strains

Another vital remit of the NCTC is to ensure that microbiologists have access to control strains, which are an essential part of the quality management system in a routine clinical diagnostic laboratory. Many strains within the NCTC are defined as authenticated control strains being recommended for use in standardised protocols by bodies, such as the World Health Organization (WHO), the European Committee for Antimicrobial Susceptibility Testing and UK Standards for Microbiology Investigations. Primary diagnostic laboratories that are conducting frontline healthcare testing require these control strains to ensure that their testing methods are performing optimally and to maintain their quality management system.

THE COLLECTION CURRENTLY HOUSES OVER:

6000 different bacterial strains

900 made up of over 900 different species

82 from 82 bacterial families

Microbiology research

From the NCTC's inception the collection has had a strong scientific focus. As well as its core functions, the NCTC has also been at the forefront of microbiology research. The first NCTC manuscript was published in 1921, only a year after the formation of the collection. Notable additional contributions include NCTC's curators Cowan and Steel's publication of the seminal manual for bacterial identification in 1965. In 1979, Dr Owen and Dr Hill were undertaking critical experiments to determine ways of calculating the genomic G+C content as a way of characterising bacterial species. This has since become used as a common marker in bacterial systematics.

The NCTC laboratories were the first in the world, in 1989, to describe applications of chelex and guanidine thiocyanate to extract DNA from bacteria. In 2012, the NCTC received a grant from the Wellcome Trust, in collaboration with the Wellcome Trust Sanger Institute, to sequence 3000 strains from the NCTC catalogue with the view to providing open source reference genomes (with a focus on type strains) to the scientific community.

Following a productive collaboration with Pacific Biosciences, 3000 long-read, high-quality reference genomes from NCTC strains are now accessible alongside the scientifically available strains. In recent years the NCTC has also ventured into performing ground-breaking proteomics studies on key NCTC strains. In 2019 the NCTC performed a study that examined the full proteomic profiles of a panel of WHO *Neisseria gonorrhoeae* antimicrobial-resistant control strains. It identified complex mechanisms that may be associated with AMR in the gonococcus that had not been previously revealed by whole-genome sequencing.

In 2020, the NCTC is 100 years old and its centenary year is an appropriate time to reflect upon its purpose and the contribution it has made to microbiology. The collection is a unique national asset and its remit has remained largely unchanged: to provide a trustworthy source of authentic bacterial strains for use in scientific studies. Currently the NCTC collection is thriving, but it is essential in order to ensure survival that it remains scientifically relevant and financially robust. It is anticipated that NCTC will continue to contribute to support scientists globally for the next one hundred years. The collection provides bacterial strains, bacterial DNA, bacteriophage and plasmids, alongside publicly accessible reference genomes to enhance the global understanding of these important pathogens. BMS

Dr Sarah Alexander is NCTC Curator and Lead Microbiologist and **Ayuen Lual** is Scientific Marketing Manager, both at the Culture Collection, Public Health England

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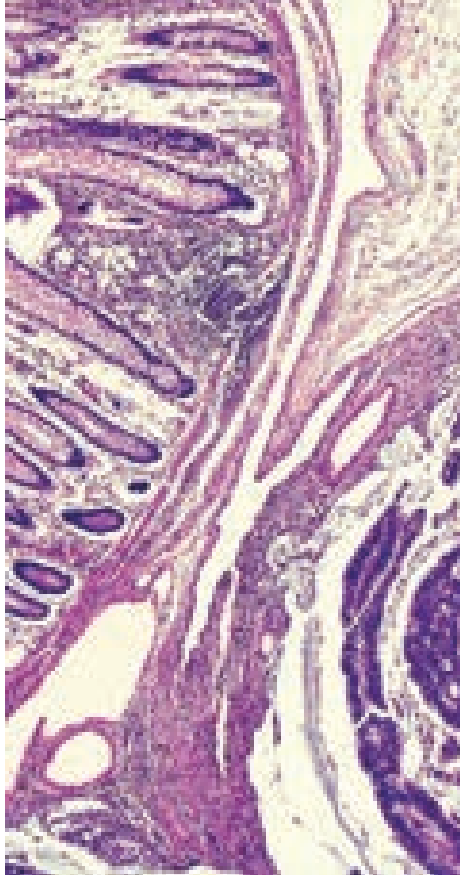


REPORTING IN HISTOPATHOLOGY

SOME PERSONAL INSIGHTS

The team at Leicester Royal Infirmary have collaborated on this article, which discusses their experiences of scientist reporting in histopathology.

Biomedical scientist reporting in histopathology started as a pilot in September 2012. By 2017 some of the scientist trainees had completed the challenging course, passed their examinations set by the Royal College of Pathologists and completed stage D of the curriculum.

Leicester was one of the first pilot centres and Lisa Wheatley is now a valued reporting scientist member of the gastrointestinal (GI) pathology team.

The value of having scientists reporting histopathology specimens as part of the team is summarised by the team members:

Consultant Histopathologist
Professor Kevin West

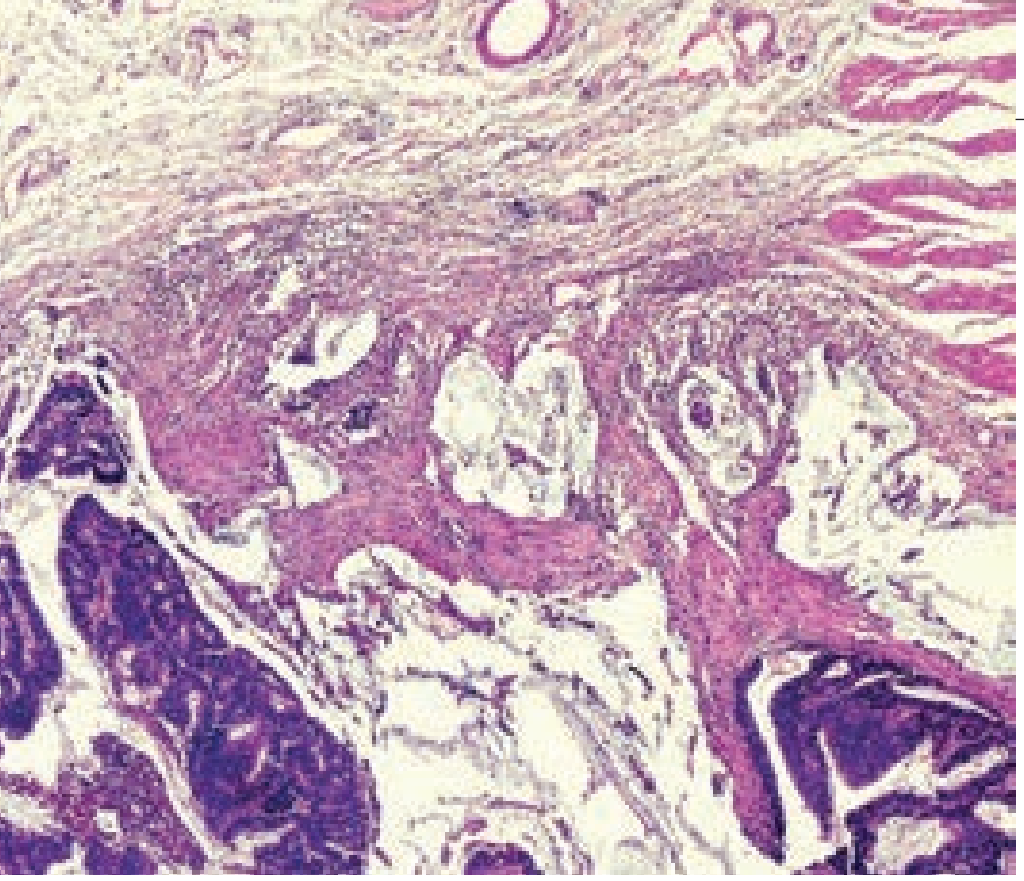
"There has been a substantial expansion of the roles of non-medical healthcare professionals since I qualified in medicine nearly 40 years ago. When fibre-optic endoscopy was introduced it was the province of doctors. Now imagine a gastroenterology service without nurse endoscopists. It would have been unthinkable for nurses to perform procedures such as carpal tunnel surgery, but this is now widely accepted. So, why not histopathology?

"I was delighted when we became a pilot centre for biomedical scientist reporting. All our GI pathologists supported the initiative and have benefited from it. An experienced biomedical scientist brings a wide range of knowledge and skills to the job, which enhances the interaction between the laboratory and medical staff, without any significant impact on the training of medical staff. The overall volume of training was not substantially altered given that, for several years, consultants had to train six ST1s starting with us every August. We have 60,000 plus specimens, so there is enough work for everyone.

"The training is, however, different. For an ST1, a substantial amount of medical knowledge may be assumed. For example, a duodenal biopsy accompanied by clinical details of anaemia should make them think of coeliac disease. That will not be so obvious to a biomedical scientist. But medical trainees will be less familiar with laboratory processes; fixation, processing and staining, the troubleshooting of which will be ingrained in the mind of an experienced biomedical scientist.

"I see scientist reporting as an adjunct to medical staff not a replacement.

"Histopathology as a profession needs to evolve and medical staff should lead teams in cellular and molecular pathology to serve the needs of patients in the rapidly developing world of precision medicine."



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Biomedical Scientist Reporter
Lisa Wheatley

"I was in the first cohort for the biomedical scientist reporting pilot, fully supported by the GI histopathologists in this department, as well as the head of service and clinical management team. I had an educational supervisor and was trained by all five GI consultants, alongside histopathology trainees, using familiar curriculum and assessment tools. I have had nothing but help from the trainees I work with; we share interesting cases and learning opportunities, even though I now have my Certificate of Completion of Training.

"I understand that there is scepticism and some hostility about the development of biomedical scientist reporting, with a perceived threat to both the histopathology profession, and to the quality of patient care. I would counter that with the fact that in this department, the role is designed to sit alongside and not replace a consultant. I release consultant time to focus on those activities and specimen types that require their specific knowledge and expertise. I have (and always will have) a low threshold for passing on cases outside my competence, and I frequently seek supervision. I present histology at multi-disciplinary team (MDT) meetings. I participate in external quality assurance (EQA) and 10% of independently reported cases are audited, as for stage D trainees.

"The advent of scientist reporters should be welcomed in the context of national recruitment and retention issues and the additional burden on histopathology posed by increased prognostics and molecular testing. It is the reporting scientist role design, and the integration of that role within existing frameworks, that needs to be carefully considered. Histopathologists are surely in the best position to do this, to shape a service that meets patient needs, and ensures the right skills are available for each part of the diagnostic process."

Junior Trainees

Training in histopathology alongside reporting biomedical scientists has been a privilege. Fundamentally, learning opportunities are increased, rather than reduced. The expertise that biomedical scientists bring to macroscopic dissection means that trainees can benefit hugely from being guided through the approach to often daunting resection specimens and commonly encountered processing issues.

Trainees also benefit from the knowledge that biomedical scientists bring regarding the mechanisms and uses of ancillary tests and provide a conduit into the inner workings of the department – an important consideration for a new starter.

Given the vast number of cases that pass through histopathology departments, the addition of reporting biomedical scientists has a negligible impact on the cases available to trainees, particularly when a culture of sharing interesting examples exists.

Senior Trainees

The biomedical scientist reporting programme has many positives for trainees – by adding additional staff to the GI team, more consultant time is freed up from macroscopic dissection, reporting workload and MDT preparation to facilitate training. Once they have made it through the initial stage of training, scientists can also train junior registrars in cut-up, reducing the burden on senior registrars and consultants. Over time, as they focus on one specialty area, they develop considerable expertise in dissection.

The scheme also promotes closer working relationships between different staff groups: the scientific staff involved gain a deeper understanding of the process of training within histopathology, and the work required, while trainee pathologists develop a better understanding of laboratory processes.

One potentially problematic area is reporting numbers; at more junior levels, in a busy department, we have found that reporting numbers for registrars are not affected. However, at a more senior level, good communication between those involved on a specialty is required to ensure training needs are met for all.

Summary

The Leicester GI team has demonstrated the significant contribution that a scientist brings to the whole reporting team. Laboratories who expand the roles of their biomedical scientists will be in a strong position to cope with the ever-increasing workload that all of us are experiencing. BMS

BRITISH JOURNAL OF BIOMEDICAL SCIENCE:

ISSUE 3 2020 – A SYNOPSIS

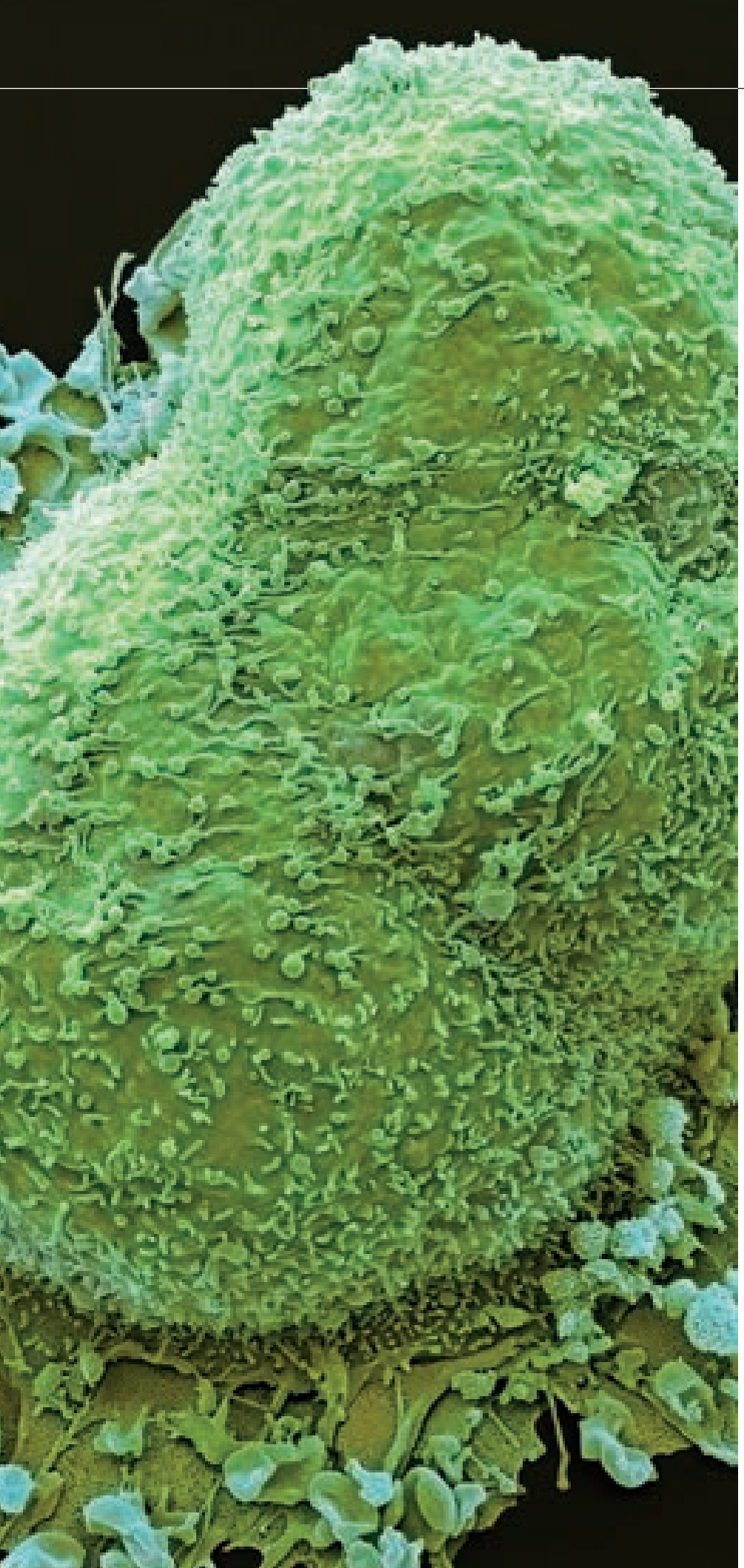
Deputy Editor Guy Orchard provides a brief glimpse of the articles on offer in the third issue of the year.

Colorectal cancer and hepatitis markers

Colorectal cancer is the most frequent type of cancer worldwide and in this issue we have a few papers investigating microsatellite instability (MSI) markers and microRNAs (miRNAs) in the pathogenesis of the disease. We start with CAT25 (T25 mononucleotide repeat of the Caspase 2 gene). T25 has been found to be a reliable marker for detecting MSI in colorectal cancer. Sanchez *et al.* attempt to develop and validate a high-resolution melting PCR (HRM-PCR) method for CAT25 instability detection in peripheral blood DNA from 110 patients with colorectal cancer, in comparison with 208 healthy volunteers. HRM-PCR for CAT25 showed a tight range of 64-66 base pairs. CAT25 results provided 100% predictive values and $p<0.0001$ to classify a tumour as having high MSI, confirming CAT25 as a promising marker for MSI analysis.

Huang *et al.* presented a paper analysing hepatitis C virus (HCV) infections and demonstrating the effects of single nucleotide polymorphisms (SNPs) of the Fas cell surface death receptor and Fas Ligand (FASL) and the impact these have in apoptosis of immune cells and target cells infected with a virus through the FA-FASL signalling pathway. Analysing four SNPs on 522 individuals with spontaneous HCV clearance and 733 patients with HCV infection. It was concluded that the genetic variant in FASL is linked with HCV infection, but not spontaneous HCV clearance.

The second paper on colorectal cancer from Abedi *et al.* investigates the upregulation of the miRNA miR-410 on prognosis of colorectal cancer patients. Assessing 120 colorectal cancer tissue specimens and 120 samples from adjoining uninvolved tissue the quantification of miR-410 expression levels was evaluated by quantitative RT-PCR. Unregulated expression of miR-410 was seen in the malignant tissue compared with normal uninvolved tissue



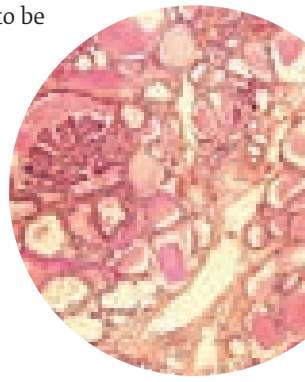
(p<0.01) with Tumour/Node/Metastasis stage and lymph node metastasis (p=0.03, p=0.004, respectively) and with worse overall survival outcomes (p=0.002). In cancer tissue miR-410 is over-expressed and is associated with unfavourable patient outcomes. It is postulated that miR-410 may be a useful tool in predicting the prognosis of colorectal cancer.

MiRNA studies in cancer and autoimmunity

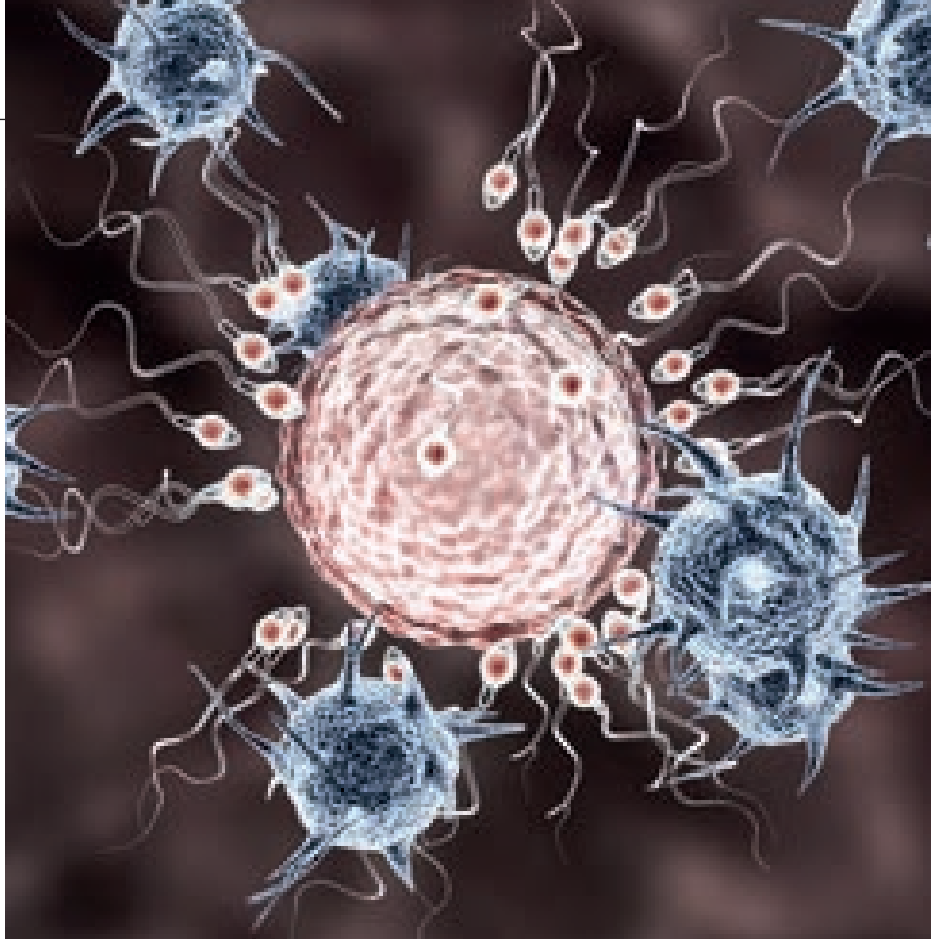
Certain SNPs in genes, such as PAD14, PDCD1 and CTLA4, are linked to rheumatoid arthritis. Here Ma *et al.* investigate the links between SNPs rs2240340, rs10204525 and rs231775 in PAD14, PCCD1 and CTLA4 in juvenile idiopathic arthritis (JIA). The three SNPs were genotyped in 150 children with polyarticular JIA and 160 normal healthy children. The findings indicated that there are various roles for these SNPs in all three genes in both the diagnosis and potentially management of children with JIA.

Papillary thyroid carcinoma (PTC) is the most frequent form of thyroid cancer and its incidence is increasing. In this study Heidari *et al.* investigate caspase-3 in the dysregulated apoptosis mechanism, believed to be central to the pathogenesis of many cancers. A total of 134 cases of PTC and 151 healthy controls were genotyped for CASP3 rs4647610 and rs4647610 and rs4647602.

CASP3 rs4647610 and rs4647602 SNPs were found not to be associated with PTC, however, rs4647610 is linked to larger tumour size and rs4647602 to lower stage of cancer.



Warford *et al.* assessed miRNAs in formalin-fixed paraffin-embedded samples of colorectal



adenocarcinoma, squamous cell carcinoma of lung, invasive breast carcinoma, and prostate carcinoma. Employing *in situ* hybridisation (ISH) and using conventional oligonucleotide probes (COP) and locked nucleic acid (LNA), the demonstration of miRNAs miR-126, miR-205 and miR-21 in prostate cancer were assessed. Similar results were obtained for the demonstration of miR-126 and miR-205. miR-21 was also successfully detected in prostate cancer. It was concluded that simplification of ISH protocols by the use of COPs provides equivalent results to the use of LNA methods also allowing precise identification of cells in which miRNAs are expressed.

Long non-coding RNAs (lncRNAs) are molecules 200 or more nucleotides in length, which can have effects on both the innate and the adaptive immune systems. Wahba *et al.* investigate long intergenic non-protein coding (linc) RNA 00305 (LINC00305), a pro-inflammatory atherosclerosis-associated lincRNA and its variant rs2850711 (A/T) in 100 cases of rheumatoid arthritis (RA) samples and compared with 100 healthy individual samples. LINC00305 genotyping and expression were assessed using allelic-discrimination PCR and quantitative real-time PCR. LINC00305 expression was significantly increased in RA patients. It was concluded that increased expression levels of LINC00305 and its rs2850711 genetic variant may well play a role in the diagnosis and patient management in RA.

A case study on post-operative infection and fertility

In this case study Long *et al.* investigate the importance of reduced sperm concentration in a patient with a suspected post-operative infection. Attention was drawn to the importance of clinical discussion and review of patient's medical history. Regular up-to-date review at each clinical step of a patient's journey is not always performed, when undergoing fertility investigations. The study highlights the importance and impact on semen quality of a post-operative infection and hospitalisation of a male patient on the fertility management pathway.

Biomedical science in brief papers

Within the genus of *Mycobacterium* there are over 160 different species. These are broadly categorised into two groups : *Mycobacterium tuberculosis* complex (MTC) and Nontuberculous Mycobacteria (NTM). Conventional and traditional methods of identification of these species have now been replaced by sequencing and proteomic methods, such as Matrix-Assisted Laser–Desorption/Ionisation time -of-flight (MALDI-tof) mass spectrometry (MS). However MALDI-tof has also been accompanied by reports of ineffective extraction methods and is deemed laborious to perform. Here we see Connor *et al.* view hypotheses on the replacement of MALDI-tof by the HAIN assay for both MTC and NTM. The GenoType CM (HAIN system) can identify MTC and some forms of NTM species. In the case of NTM, timely identification of the species responsible is important for choosing a suitable antimycobacterial therapy. The study demonstrates the clinical utility of MALDI-tof MS for the identification of mycobacteria using a two-step cell disruption protocol. The authors suggest wide-scale implementation of MALDI-tof MS using the two-step cell disruption protocol will help future-proof clinical laboratories against a background of increasing rates of NTM infections.

Finally Sediq *et al.* investigate TNFSF15 in Behcet's disease. Behcet's disease is a chronic multi-systemic disorder of relapsing mucocutaneous, ocular, vascular and central nervous system manifestation with vasculitis. Sediq *et al.* investigate the theory that altered TNFSF15 (rs3810936) polymorphism distribution, as well as different peripheral blood TNFSF15 expression, is involved in the pathophysiological mechanism in Behcet's disease. The authors point to the roles of TNFSF15 genotypes and production of IL-6 and TNF-alpha by LPS-stimulated peripheral blood mononuclear cells. It is suggested that TNFSF15 (rs3810936) polymorphism is important in the pathophysiology of Behcet's disease and its effect on clinical presentation.

CPD

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

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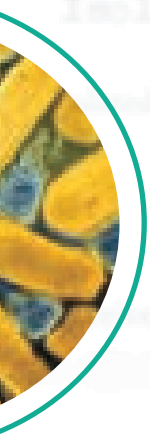
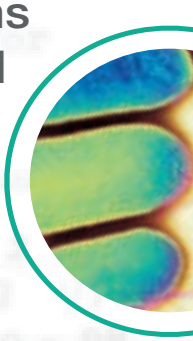
NCTC

The National Collection of Type Cultures

National Collection of Type Cultures
100TH Anniversary
NCTC
Operated by Public Health England



Established in 1920, the UK's National Collection of Type Cultures is one of the longest established collections of medically relevant microorganisms in the world. It is a global provider of authentic bacterial strains and associated biological materials to the international biomedical, research and quality control community.



Products

Over 5500 strains of bacteria including historic, contemporary and antimicrobial resistant isolates

Strains specified by quality control guidelines such as EUCAST and UK Standards for Microbiology Investigations

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Services

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Bespoke DNA extraction and LENTICULE® Disc production

A recognised collection that supports the description of novel bacterial species

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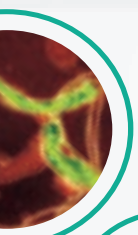

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HOW TO... MAKE THE MOST OF AN INTERNSHIP

Kamila Orzechowska, a second-year student at Coventry University, writes about her experiences of a research internship and advises how others can get the most out of work experience.

I have been interested in science for as long as I can remember. I have undertaken several courses around science and biology and am currently studying Biological and Chemical Sciences at Coventry University. My ultimate ambition is to translate into an accredited Institute of Biomedical Sciences (IBMS) programme, where I can advance my laboratory practice and skillset, focusing on medical microbiology.

Due to COVID-19, I found it challenging to identify a placement, but was signposted to the work of the Renal Patient Support Group (RPSG) and, over the summer, I have been building my healthcare science knowledge around kidney care and laboratory practice, developing understanding of science and research. I think it is important to be a pragmatic and resourceful scientist for healthcare practice and the RPSG has been amazing in helping me to become a rounded young scientist professional.

The RPSG was founded in 2009 with the view to provide online peer support and education for patients suffering with Chronic Kidney Disease (CKD) in the UK. Whilst it started with baseline mild affiliation with the North Bristol NHS Trust, it has expanded to a global membership.

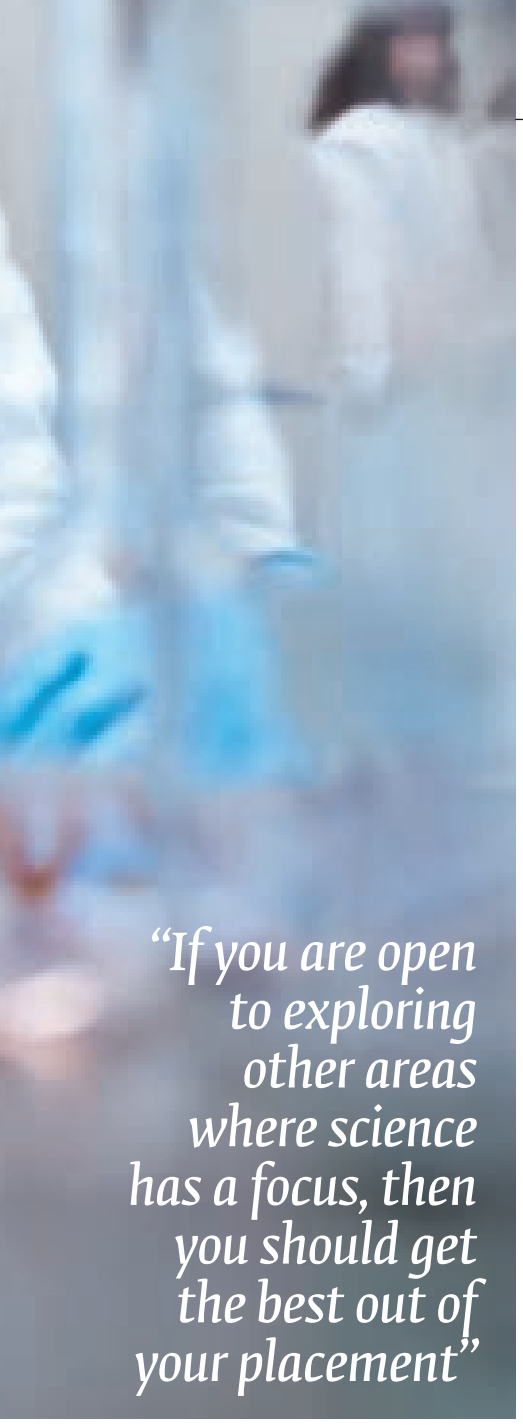
The RPSG is an evidence-based support group, where patients and carers have opportunities to share real-life experiences. I have been amazed by the fantastic team and leadership this group has. The efforts really highlight opportunity for discussions and how patients, professionals and researchers can work together to find answers to important questions, improve healthcare treatments, quality of life and life expectancy. My time has provided me with a good understanding of how biomedical sciences can be involved to support smarter care for CKD patients with probable comorbidities and multimorbidity.

Developing skillsets

This experience has helped me in developing the necessary skills to be a biomedical scientist. I am learning about lab practices, engaging with academics, researchers and wider health professionals. I am learning about new areas of care relating to kidney disease and gaining an understanding of how important involvement of healthcare scientists really is in patient care whilst contributing to frontline practice.

I have been able to increase my knowledge of kidney pathology, primary care, secondary care, different terminologies, care plans and treatments. I have also contributed to webinars and virtual conference calls under supervision.

I would like to develop my final-year



"If you are open to exploring other areas where science has a focus, then you should get the best out of your placement"

dissertation project under RPSG supervision surrounding polycystic kidney disease (PKD), and I am currently developing the proposal. Also, I would like to explore areas of medical microbiology surrounding PKD. I would like to eventually have a biomedical science career in microbiology. Together, with my internship supervisor, I am hoping to present a snapshot of my final year project in the form of a poster presentation at the IBMS Congress in 2021, and would like to get this work published in affiliation with the RPSG after my dissertation is completed. All this experience has taught me how to combine biomedical science and research.

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Internship activities

Following my internship, I am looking to transfer onto an accredited IBMS programme. My internship with RPSG has involved several activities, including preparation of and participation in a webinar surrounding polypharmacy and renal biomarkers. Working on my presentation, I developed a general understanding of polypharmacy, renal insufficiency and nephrotoxicity. I also gained an understanding of risk factors for patients with CKD.

The webinar was collaborative and, with my internship supervisor, I presented insights on biomarkers to an international online audience. This helped me gain confidence, and the importance of clear communication. As part of this work, I was also invited by my internship supervisor to co-create a poster presentation titled *Polypharmacy and Nephrotoxicity: Understanding the Problem and Prompting Early Renal Screening for Best Practice – Review*. This poster communicates how to avoid excessive, inappropriate, or inadequate prescribing in the elderly population living in care and nursing homes.

My internship has motivated me to work and strive to become a well-rounded scientist and professional and to embrace the concept of "more than science in the laboratory".

I am also privileged to have helped in developing three collaborative papers, which are being prepared for publication. I am now looking to get involved in further collaborative research work.

Advice for others

Searching for a placement is a long process. It was a struggle to find work in a laboratory setting to build on my biomedical science skills. One of the best ways to search out placement opportunities is to explore different areas of healthcare where biomedical science has an important focus.

It is about connecting – writing letters and approaching people who may have links. You might not get what you originally plan for, but science, it is about being open to learning and wider opportunities.

It is important as a developing scientist to make transparent what you want. It is good to be proactive and open to learn new things and it is vital to act professionally at all times. I referred to the IBMS Good Practice guideline (2017) and that gave me a good idea of professional conduct in and outside the laboratory environment.

Searching took me in many directions, but getting the most out of your placement is about showing your understanding as part of the interview process. You want to be in a position where you can learn and develop and link that back to your undergraduate education. If you are open to exploring other areas where science has a focus, then you should get the best out of your placement. BMS

MY IBMS NEWS

LEADERSHIP

SEVEN MAKE THE POWER LIST

This year, seven IBMS members were awarded places on *The Pathologist*'s power list.

The publication says the list is comprised of "inspirational individuals who make laboratory medicine such a fantastic field". The seven are:

Cherie Beckett – Biomedical Scientist in Microbiology at the Princess Alexandra Hospital NHS Trust in Harlow.

Matthew Burdett – Medical Technical Officer at Unilabs in London.

Ian Davies – Senior Lecturer at Staffordshire University.

Jo Horne – Advanced Practitioner Healthcare Scientist in Cellular Pathology at University Hospital Southampton NHS Foundation Trust.

Hayley Pincott – Associate Practitioner in the Oral Pathology and Microbiology department at Cardiff and Vale University Health Board.

Malcolm Robinson – Retired biomedical scientist and founder of the charity Harvey's Gang.

David Wells – biomedical scientist working as Head of Pathology at NHS England's COVID-19 Testing Cell.

OBITUARY

George Hunt FIMLS (1922–2020)

George Hunt was the Senior Chief MLSO in Microbiology at the Queen Elizabeth Hospital for Children, Hackney Road – a hospital he served for around 40 years. Later he became the Principal MLSO for the Hospitals for Sick Children, which included Great Ormond Street Hospital.

George was an "old school" microbiologist, working with great care and expertise. He gave meticulous attention to obtaining the best results possible from small paediatric specimens. He also enjoyed research and was never happier than when investigating something unusual that he had noticed on the bench. As well as publishing articles on a variety of microbiological subjects, he was knowledgeable in other pathology disciplines, particularly clinical biochemistry.

He was an excellent amateur artist and also enjoyed poetry (especially Keats). He made wine, picking the fruit himself. Heraldry was another interest and he designed his own coat of arms and investigated his family tree.

During the war, he narrowly missed being drafted to a hospital where all the patients and staff were killed. He also served in India. At one time, he was on the small air-sea rescue boats, picking up pilots whose aeroplanes had ditched into the sea.

George died peacefully at home with his family. He leaves Sylvie, his wife for over 60 years, his daughter Gillian and grandsons Alan and Peter.

→ **Elizabeth Price**

MEMBERSHIP

TAX RELIEF ON FEES

If you are a UK taxpayer you can save money by claiming tax relief on your IBMS membership fees.

If it's your first time claiming tax relief, you can include a backdated claim for the previous four tax years.

The amount you'll receive depends on your membership fees and your tax situation. Savings range from £6.80 per year for retired members to £35 per year for fellows.

→ **Find more information, visit ibms.org/join/tax-relief**

CAMPAIGNING

SHOWCASE MEMBERS' ROLES

The Science Council is calling for IBMS members to help "showcase science" during the COVID-19 pandemic.

It is launching a new blogging campaign and is inviting contributions from IBMS members.

→ **If you would like to take part, email communications@ibms.org with your name, NHS trust or association of work and the details of the story you would like to share.**

JOURNAL-BASED LEARNING EXERCISES

IBMS Institute of Biomedical Science
Continuing Professional Development

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

DEADLINE WEDNESDAY 2 DECEMBER 2020

Position paper on International Collaboration for Transfusion Medicine (ICTM) Guideline 'Red blood cell specifications for patients with haemoglobinopathies: a systemic review and guideline'. Trompeter S, Massey E, Robinson S; Transfusion Task Force of the British Society of Haematology Guidelines Committee. *Br J Haematol* 2020; **189**: 424–7. Assessment No 080220

01	The International Collaboration for Transfusion Medicine Guidelines was established in 2010 and includes international experts.	11	Many adults in the UK who are on long-term transfusions for SCD are treated on automated exchange where the regime can vary from six to eight weekly and need 8–12 units a time.
02	The British Society for Haematology Guidelines Committee has four taskforces.	12	The donor population in England is less than 88% Caucasian, therefore matching large quantities of blood for these antigens routinely is feasible.
03	The first recommendation is aimed at patients with sickle cell disease (SCD) who have one or more clinically significant antibodies.	13	Patients may have their transfusions delayed if blood is requested beyond their Rh and K antigen match.
04	The first recommendation also states that patients should be transfused with CcEe- and K-matched red blood cells.	14	Blood services are striving to increase donations from black and minority ethnic groups.
05	The 2013 BSH guidelines recommend that the patient's RBC phenotype but not genotype should be known prior to transfusion.	15	The fourth recommendation is aimed at patients with thalassaemia syndromes who have only one or more clinically significant alloantibodies requiring transfusion support.
06	Phenotyping patients is a cheaper option that genotyping, and is only carried out at one site: IBGRL, Filton, Bristol.	16	Provision of blood which is CcEe-, K-, Fy^a-, Fy^b-, JK^a-, Jk^b, Ss-matched is not current UK guidance or BSH guidance for patients with thalassaemia who have one or more alloantibodies.
07	The second recommendation is for patients with sickle cell disease who have one or more clinically significant antibodies to be transfused with antigen-negative blood.	17	Alloimmunisation of patients who have thalassaemia with one or more alloantibodies is often caused by Rh and Kell antigens and is usually due to historical transfusions prior to recommendations for Rh and Kell matching.
08	BSH guidance on compatibility has previously recommended that red cells provided for transfusion should be antigen-negative for all antibodies.	18	Development of further antibodies in transfusion-dependent thalassaemia patients occurs more commonly than patients in the sickle cell cohort.
09	BSH guidance states that patients should be informed of their antibody status and be given a card to notify health workers.	19	A precision transfusion model could be applied to each patient if whole-genome sequencing of donors and patients is introduced, creating more stringent matching.
10	The third recommendation for patients with SCD who have one or more alloantibodies should be transfused with CcEe-, K-, Fy^a-, Fy^b-, JK^a-, Jk^b- only red blood cells to reduce the risk of alloimmunisation.	20	The ICTMG guidance focuses on the age of blood as well as the provision of HbS-negative units.

REFLECTIVE LEARNING

01	Compare the terms phenotype and genotype.	02	Discuss the benefits and accompanied limitations of extended phenotyping for new SCD patients.

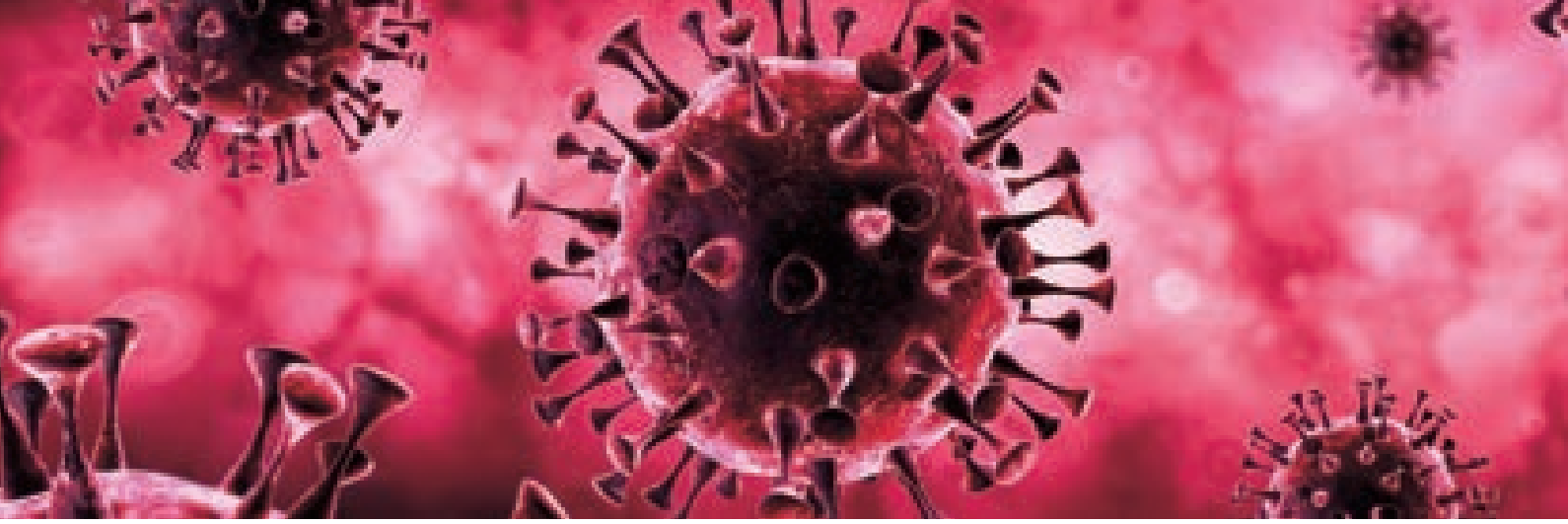
DEADLINE WEDNESDAY 2 DECEMBER 2020

Digital pathology in the time of corona. Stathonikos N, van Varsseveld NC, Vink A *et al.* *J Clin Pathol* 2020 Jul 22; jclinpath-2020-206845. doi: 10.1136/jclinpath-2020-206845. Online ahead of print (https://jcp.bmj.com/content/early/2020/07/21/jclinpath-2020-206845). Assessment No: 080720

01	Submitted specimens and autopsies need to be treated as potentially infectious.	11	A digital diagnostic workstation included a 3D mouse and multiple screens, of which a 27-inch, 4k display with an IPS panel was used as the main image viewer.
02	The UMC Utrecht started to build up a digital pathology infrastructure in 2018 based on three Leica Aperio scanners, a tape storage system and a custom in-house-developed image integration software.	12	During the multidisciplinary meetings that are often done by another pathologist than the one signing out, including full review of all cases to be discussed, no errors attributable to working from home have been detected in the first six months.
03	UMC Utrecht has amassed a complete digital archive of scanned histology slides over the last two years.	13	Pathology residents were also divided into two teams that would work week-on/week-off on the premises and from home. In each team, junior and senior residents were equally represented. The supervising pathologist kept in touch with both teams to coordinate activities.
04	The scanned slides are added to the correct case, based on the barcode information alone.	14	The residents would not place annotations and comments on the digital slides, which could be reviewed by the supervising pathologist, and created the pathology reports by structured reporting or keyboard.
05	The UMC Utrecht PACS holds all images of diagnostic cases from the department, including order forms, and macro, electron microscopy, immunofluorescence, autopsy and fluorescence *in situ* hybridisation (FISH) images.	15	Meetings were replaced by video conferencing (Zoom, later WebEx because of security concerns), including the monthly staff and diagnostic meetings.
06	The PACS employs a direct archive access protocol that permits us to view the archived cases without the need to retrieve them from archive (an otherwise time-consuming operation), which effectively forbids us to access the history of a patient since 2008.	16	The removal of tubes and lines was preferably performed on the ward before moving the patients to the morgue.
07	The 2020 COVID-19 crisis did not force us to quickly come up with a new way of working, based on international standards and social distancing, even within the department.	17	If the COVID-19 status of the autopsy patient was evident, we considered the patient positive and took precautionary measures according to our protocol of infected autopsies.
08	Working from home was facilitated through a VPN connection.	18	The molecular findings were reported in the pathology reporting system. If any feedback was necessary (eg reflex testing), this was mentioned in the digital molecular authorisation list, which was regularly checked.
09	Passage between the reception desk and grossing room was restricted to avoid cross-contamination and was only used for transfer of primary specimen containers and forms. All forms were digitised and made available via the PACS and were stored afterwards in this reception area.	19	The wish list to further optimise the home-working space consisted of the sync between the PACS and pathology reporting system (UDPS), speech recognition, a 3D mouse, higher image retrieval speed and higher screen resolution.
10	Medium-risk and high-risk tissues were fixed in formalin for at least 24 hours and further initially dissected (eg opening bowel specimens) while submerged in formalin.	20	Although there were certainly disadvantages for family life by being much more at home (with less morning stress for those parents with young children), some faced higher stress having to work at home with the kids around, day care facilities being closed.

REFLECTIVE LEARNING

01	Reflect upon the changes the coronavirus pandemic has brought on your department.	02	Consider the potential changes required for your department to migrate to digital pathology.



Molecular diagnostics for respiratory diseases including COVID-19 and the next Flu season

Amplidiag® COVID-19 (CE-IVD) Batch testing

Sample type	Nasopharyngeal swab
Technology	RT-PCR
Targets	SARS-CoV-2 (orf1ab) SARS-CoV-2 (N)
Time to results	Amplidiag®: Amplification 55min/<3h (including extraction and PCR set up with Amplidiag® Easy) Novodiag®: About 1 hour direct from sample

Novodiag® COVID-19 (CE-IVD) On-demand testing

Advantages:

- A **complete solution** for rapid diagnostics of novel coronavirus infection
- A test for **all sample volumes (batch or on-demand testing)**
- Mobidiag offers **"sample to result" solutions** with robust supply lines to **ensure continuity of testing**

COMING SOON

RESP-4

2 molecular tests for batch testing or on-demand testing for simultaneous detection of

COVID-19, Flu A, Flu B, RSV

Please contact us for more information or visit www.mobidiag.com

MOBIDIAG

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sales@mobidiag.com

How did diagnostic companies such as Mobidiag support the fight against the coronavirus and prepare for what's coming next

As the coronavirus pandemic unexpectedly took hold around the world, it quickly became apparent that there was an urgent need for fast, safe and accurate diagnostic solutions for COVID-19 infection to support clinical decisions, improve patient care and support pandemic control.

At Mobidiag our immediate response was to harness our existing technologies and expertise, including supply chain management and manufacturing, to rapidly develop and supply new molecular tests for detection of the SARS-CoV-2 virus.

A complete molecular offer for the detection of SARS-CoV-2

Thanks to its strong expertise in molecular diagnostics, Mobidiag team has mobilised and has brought to the market in a timely manner two complementary RT-PCR diagnostic tests for the detection of COVID-19. Both tests are CE-IVD and detect two distinct genes (orf1ab and N) in accordance with the regulations.

- **For batch testing: Amplidiag® COVID-19**

Amplidiag® COVID-19 test is a real-time RT-PCR kit which allows DNA amplification in 55 minutes directly from nasopharyngeal swabs. The entire process (extraction and preparation of PCR plates) can be automated with the Amplidiag® Easy platform or other compatible systems for high-throughput screening requirements.

- **For on-demand testing: Novodiag® COVID-19**

Novodiag® COVID-19 test operates using the Novodiag® rapid and easy to use 'sample-in, result-out' system. It allows the fully automated detection of novel coronavirus in approximately 1 hour (<5min hands-on time) from nasopharyngeal swabs. Novodiag® is a closed system ensuring the protection of healthcare professionals from possible contamination.

Supporting hospitals and clinical labs in United Kingdom

It has been widely reported that there is a shortage of raw materials required for the mass production of coronavirus diagnostic tests, as well as consumables needed throughout the global diagnostic workflow. This is a direct result of the current environment and the high demand for these tests.

To combat this, Mobidiag has worked to ensure that its supply chain and manufacturing capabilities are robust and able to support its customers across the breadth of our offering. We have established in-house manufacturing and sourcing and have acquired the various consumables needed to cover the complete workflow from sample collection to results, allowing us to be self-sufficient in production of our COVID-19 tests. As a result, both Amplidiag® and Novodiag® solutions have been adopted by a range of laboratories in the UK to help meet the demands of testing.

Preparing for the next flu season

Needless to say that COVID-19 has led laboratories and industries to adapt quickly. As a result, all healthcare professionals are preparing for what may come next. We, at Mobidiag, have been acknowledging the need for new tests. We have been anticipating and are currently developing new molecular tests allowing simultaneous detection of SARS-CoV-2, RSV and Flu A and B. Similarly to our current COVID-19 tests, 2 tests will be available for different volumes requirements: batch testing and on demand testing. Both tests are currently under development and releases are expected for the next flu season.

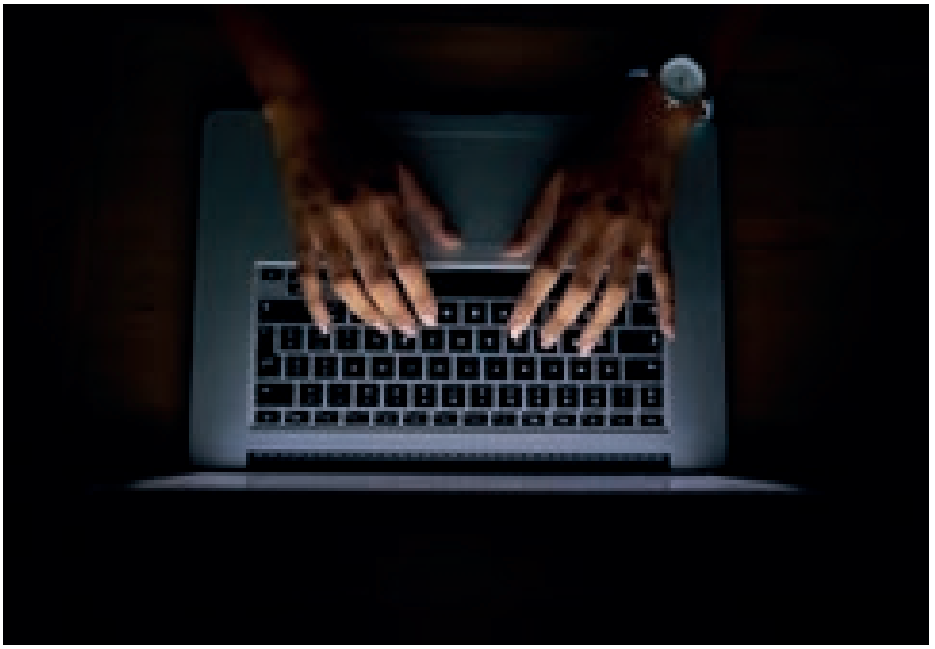
For more information, please visit www.mobidiag.com or contact us at sales@mobidiag.com.

MOBIDIAG

HERE TO HELP

NEW CYTOLOGY PORTFOLIOS

This month we are outlining a new launch to better support the training and development of the biomedical scientist workforce.



The IBMS is committed to ensuring that our qualifications reflect service changes and needs. We provide training programmes and qualifications that are directly relevant to staff working in biomedical science laboratories and at all stages of the career pathway. These include biomedical scientist post-registration qualifications in discipline-specific practice, our range of Specialist Diplomas.

In light of the increasingly specialised biomedical scientist roles focusing mainly on either cervical or diagnostic fields of cytology, the IBMS Cytology Advisory Panel made the decision to totally review and relaunch the cytology Specialist Portfolios to better reflect the more focused services now provided by laboratories. The changes also reflect the increasing role molecular-based techniques are playing across pathology as a whole and increasingly so within cytology.

The outcome of the review is two new cytology portfolios in cervical and diagnostic cytology that have evolved from the previous combined version. Additional elements have been added to both fields to reflect the expansion of expected knowledge now required. This can be seen most noticeably within the diagnostic cytology version.

Individuals successfully completing one of the new cytology portfolios will be awarded a Specialist Diploma in either Cervical or Diagnostic Cytology. For the small number of individuals who continue to work in laboratories that provide both cervical and diagnostic services, there is the option to complete both portfolios at the same time or separately and then to receive two separate Specialist Diploma awards if they are assessed to have met the required standards within each portfolio. A separate assessment will be required for each version. There may be elements within each portfolio that are not part of a laboratory's repertoire; in these instances, the candidate must ensure the knowledge elements are fully evidenced. Training officers and managers are encouraged to provide candidates with practical experience to support the required knowledge elements that may involve a visit to another laboratory to experience the practical application of elements not handled in their own department.

The review outcome is new portfolios in cervical and diagnostic cytology

The new portfolios will be released early in September 2020 and can be applied for via the usual process for ordering Specialist Portfolios – ibms.org/education/specialist-qualifications/specialist-diploma.

It is hoped that these new portfolios will better support the training and development of our biomedical scientist workforce as we operate in new and different ways.

IMAGES: ISTOCK

NEW LABORATORIES NEW OPPORTUNITIES

CELLULAR PATHOLOGY ROLES WITH HSL

HEALTH SERVICES LABORATORIES

Our new laboratories at 60 Whitfield Street form one of the largest Cellular Pathology departments in the UK. They incorporate Histology, HSL-Advanced Diagnostics and Diagnostic Cytology, serving five NHS hospital sites. Following this transformation and expansion we have vacancies for BMS and Senior BMS staff, offering opportunities to become part of this new and prestigious site. For the Senior roles, we are looking for experienced dissectors, but there would also be the chance to train in dissection techniques if you are an experienced and fully qualified BMS.

The new laboratories, equipment and IT solutions have all been designed, procured and developed by HSL staff, to create a modern, safe and comfortable working environment. We are planning a lean, specialty based approach to team working to provide an efficient service, which processes over 120,000 requests each year. Research and development support complements and runs alongside our diagnostic service.

We are committed to career progression and training support for all grades, from support staff, through to specialist roles including BMS dissection and reporting. HSL has its own Education Faculty with a commitment to support training and education activities such as preparation for portfolios, attendance at meetings and conferences, and higher education activities such as study for MSc degrees. In addition we have departmental links with Quality Management, Health and Safety, Training and IT - meaning there are opportunities to expand your knowledge, follow your specialist interests and cultivate a successful career as a BMS.

You can find information on all roles at HSL by visiting - **www.hslpathology.com/careers**

MY LAB

A MULTI-DISCIPLINARY LABORATORY WITH A FOCUS ON QUALITY

Lynnette Garrett, Laboratory Medicine Quality Manager, gives a guided tour of the services at Swansea Bay University Health Board.

The Swansea Bay University Health Board (SBUHB) laboratory medicine team provides services for the Swansea and Neath Port Talbot areas in South Wales. The health board serves a population of around 390,000 and employs approximately 12,500 staff.

The laboratory medicine service provides a multi-disciplinary clinical laboratory service across four hospital sites and includes the disciplines of clinical chemistry, laboratory haematology, blood transfusion, cellular haematology, serum protein analysis, immunology, POCT and toxicology. We also manage four sample reception areas, the phlebotomy service and a cross-site courier service.

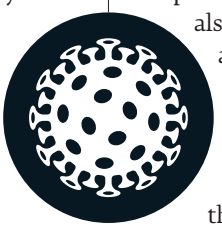
The service includes a main hub site and two satellite laboratories, with all three laboratories providing a 24-hour service and offering regional testing for some specialist tests.

Each hospital site has its own clinical specialties, including emergency medicine, cancer services, maternity, regional renal centre, regional cardiac centre and regional burns and plastic centre. Our staff experience the varied requirements that go hand-in-hand with each of these specialties.

In recent years we've been very successful in getting staff through the registration portfolios, as well as staff completing MScs, leadership qualifications and professional doctorates. We also have placement students from Cardiff Metropolitan University's healthcare science course.

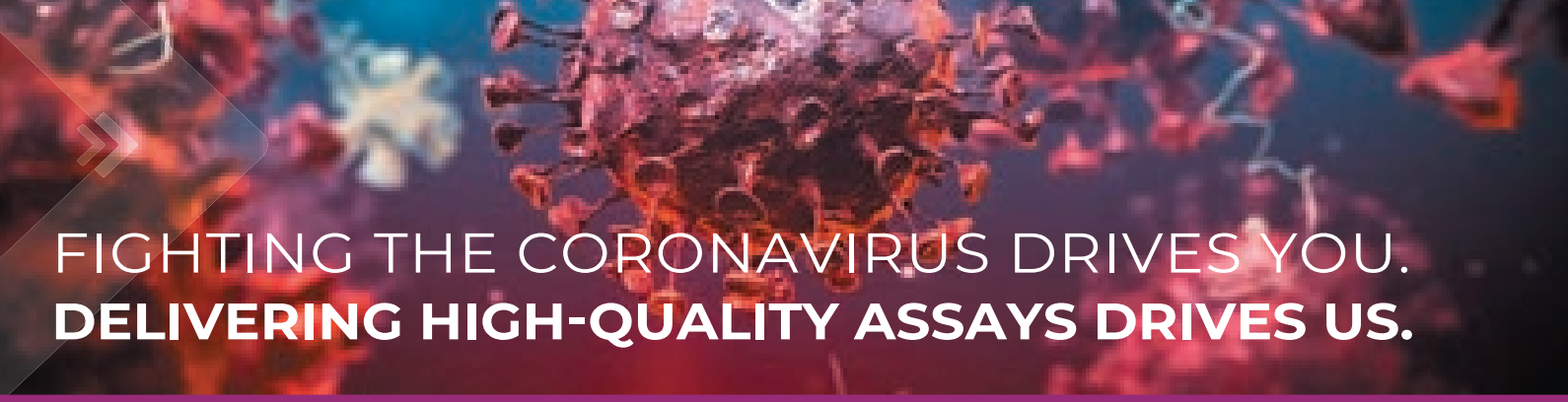
Our lab has a real focus on quality, with our services being accredited to ISO 15189 and plans well under way for ISO 22870 accreditation for our POCT service.

An article describing a laboratory service at this time would not be complete without discussing COVID-19 testing. The laboratory is now testing COVID-19 antibodies, with a peak testing of 2000 requests a day. This put us under pressure, but we adapted to turn around the samples quickly as well as maintaining our normal work turnaround times.



SBUHB pathology has received several nominations in the 2020 AHA ESTEEM awards, including for our work supporting the health board's field hospitals, phlebotomy and POCT during the pandemic. In recent years we've also won local chairman's awards for our research and development team.

Our laboratory service continues to thrive, driven by quality and innovation, to meet the need of our users. BMS



FIGHTING THE CORONAVIRUS DRIVES YOU. **DELIVERING HIGH-QUALITY ASSAYS DRIVES US.**

ACCESS SARS-COV-2 IGG ASSAY

Integrate **high-quality antibody testing into your routine workflow, regardless of the size of your lab** to help identify front line healthcare providers, patients, and community populations who have potentially developed an immune response to the SARS-CoV-2 virus.

ACCURATE, RELIABLE RESULTS HIGH IN MEDICAL VALUE

The Access SARS-CoV-2 IgG assay detects antibodies to the receptor-binding domain (RBD) of the spike protein.

Studies have shown that antibodies against the RBD are neutralizing in vitro, indicating that they may be an effective measure of immunity when compared to antibodies against other SARS-CoV-2 viral proteins*.

SUPPORTING DATA & RESULTS

200 Tests an hour can be run on DxI 800, one of the highest throughput analyzers in the market.

Also runs on DxI 600 (100 tests/hour and Access 2 (50 tests/hour). Runs in Random Access Mode seamlessly integrating into current lab workflow without the need for batching or special maintenance. The Access SARS-CoV-2 IgG assay has 200 tests per kit, requiring less frequent ordering.

100%
SENSITIVITY

99.8%
SPECIFICITY VALIDATED AGAINST 1395 SAMPLES

200
TESTS AN HOUR CAN BE RUN ON DXI 800

ASSAY CHARACTERISTICS:

2 STEP
ASSAY

RESULTS
IN **~25 MINUTES**

28 DAYS
ONBOARD CALIBRATION

SOLUTION

Generate accurate and reliable results that clinicians can trust for individualized patient care, with market-leading assay sensitivity and specificity that can be integrated seamlessly into routine laboratory workflow.
Learn more at www.beckmancoulter.com/coronavirus

*References:
Human monoclonal antibodies block the binding of SARS-CoV-2 spike protein to angiotensin converting enzyme 2 receptor: www.nature.com/articles/s41423-020-0426-7
Establishment and validation of a pseudovirus neutralization assay for SARS-CoV-2: www.ncbi.nlm.nih.gov/pmc/articles/PMC7144318

BECKMAN COULTER

I KNOW WE ARE SAVING LIVES

THE POWER OF KNOWING

Roche Diagnostics gives you The Power of Knowing that you're using accurate information to make the right decisions today, so your patients can experience a healthier tomorrow.

Roche