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APRIL 2020

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CONTENTS

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EDITORIAL

NEWS

OPINION

SCIENCE

COVER FEATURE

ADVICE

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THE EMERGING PANDEMIC

In times of panic and hysteria, we need to look at the evidence and listen to the scientists.

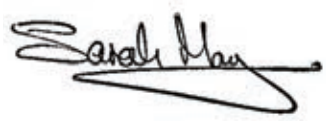
At the time of writing this editorial, every news item and conversation seems to involve the coronavirus pandemic. It's hardly surprising, because a pandemic is something most of us have never experienced and, in our health and safety-conscious culture, we are socially and mentally unprepared for something that has such potentially widespread risk to our freedom and wellbeing. Mass fatalities are something that happens to other people and societies, not us. Not here in our safe and sophisticated culture.

For me, and many others, the most unnerving thing is the speed with which the infection prevalence, and accompanying government advice, is changing. I know that by the time this edition of *The Biomedical Scientist* is published, we will be in a different and more threatening situation than we are at this moment. If the scientific modelling is correct, we are only three weeks behind Italy in terms of disease spread and impact, and life is about to change beyond all recognition for most people. It is beginning to dawn on everyone that this is an exceptional situation that will last way beyond a couple of weeks and whose effects will be felt for months, if not years.

As usual, I am irritated by negative and sensationalist reporting; the general public, and journalists in particular, seem to have a major problem in accepting scientific and medical advice and seem to value the opinion of absolutely anyone over the scientific evidence of pandemic modelling. I wanted to applaud Jurgen Klopp who, when asked his opinion about the measures being taken to cancel sporting fixtures, responded: "I wear a baseball cap and have a bad shave. My opinion is really not important." I believe that the best advice will be based on scientific evidence but unfortunately the actual actions may well be based on a mixture of public pressure and hysteria. I'm just waiting for the snake oil peddler to come motoring into town.

Unfortunately, the consequence of the hysterical reporting and doomsday prophets is the emergence of hoards of selfish individuals, building their own personal bunkers out of toilet rolls and hand sanitiser bottles. Thankfully, they are more than matched by those who are offering their services to help others more vulnerable in their communities and, as usual, our healthcare workers are rising to the challenge. I know the heroes will be the doctors and nurses but I'm hoping journalists will realise the massive contribution that our scientists are making to help in this unprecedented situation. What a contrast; the takers and the givers.

As a final thought, from the summit of my scientist's soap box, has anyone else noticed that all disaster movies start with a scientist being ignored?



Sarah May
Deputy Chief Executive

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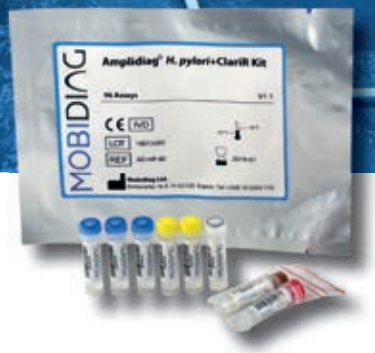

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SCIENCE NEWS IN NUMBERS

29

COUGHS AN HOUR

Up to 10% of adults experience "chronic cough" symptoms with no clear underlying cause.

In a clinical trail, **453 men and women** reported that they coughed **24-29 times an hour**. Following a **12-week trial with a potential new drug**, this fell to an average of **11 times an hour**.

Winter delays

In December and January:

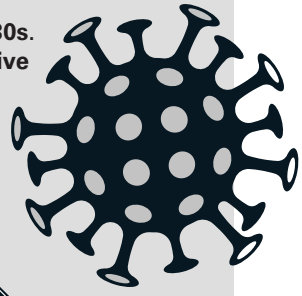
1 in 5 **walk-ins at A&E** waited for **more than four hours** to be seen.

1 in 7 people **waited over 30 minutes** to be handed over to A&E staff when **arriving at hospital by ambulance**.

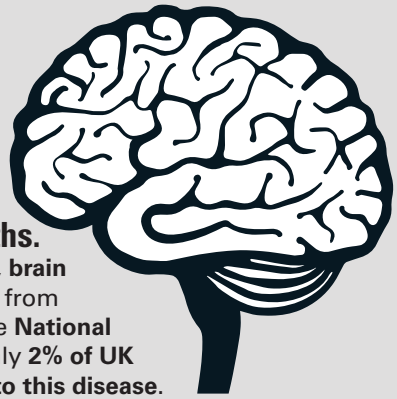
x10 RISK FOR ELDERLY

In the first big analysis of more than 44,000 coronavirus cases from China, the death rate was x10 higher in the very elderly, compared with the middle-aged.

The **death rates were lowest** for the **under 30s**. Deaths were at least **five times more common** among people with underlying health conditions.



2% OF CANCER RESEARCH FUNDS



For the under 50s, brain tumours account for one in 10 cancer deaths.

For **children** (those aged under 15 years), **brain tumours account for one in three deaths** from cancer. But, according to figures from the **National Cancer Research Institute for 2018-19**, only **2% of UK cancer research investment is allocated to this disease**.

Expensive cars are the least likely to stop for pedestrians. Of 461 cars that US researchers examined, only 28% stopped at flashing pedestrian crossings.

The **odds of stopping decreasing by 3%** per **$1000 increase** in the **car's value**.

SCIENCE NEWS

POCT

BLOOD TEST FOR ALZHEIMER'S

A point-of-care blood test is being developed to swiftly reveal if a patient with memory issues has Alzheimer's disease or mild cognitive impairment.

The test can also distinguish both conditions from frontotemporal dementia.

If approved, it could lead to a jump in the number of Alzheimer's patients enrolling in clinical trials and be used to monitor response to those investigational treatments.

In a new study, scientists measured blood levels of phosphorylated tau 181 (pTau181) – a brain protein that aggregates in tangles in patients with Alzheimer's.

It was 3.5 times higher in people with the disease compared with healthy peers.

In contrast, in patients with frontotemporal dementia, a condition often misdiagnosed as Alzheimer's, pTau181 was found to be within the same range as the control group.

Senior author Adam Boxer said: "This test could eventually be deployed in a primary care setting for people with memory concerns to identify who should be referred to specialised centres to participate in clinical trials or to be treated with new Alzheimer's therapies, once they are approved."

Diagnosing Alzheimer's disease at early stages "may be especially beneficial to patients with mild cognitive impairment".

→ **go.nature.com/3cljVhx**

STROKE

Reducing deadly brain swelling

Cases of potentially deadly brain damage as a result of stroke could be reduced after new research identified a pathway in the brain that causes swelling, and which responds to an innovative treatment.

Research led by the University of Exeter reveals how a malfunction in the way key proteins are transported within the brain after a stroke can lead to swelling, which can cause severe damage.

The international team has developed a compound that effectively treats this pathway in laboratory tests, paving the way for a new treatment.

This could potentially provide an alternative, more effective way to treat brain swelling, for which currently there are limited treatment options.

Stroke is typically caused by a blood clot in the brain and can lead to death within minutes. In the UK alone, more than 100,000 strokes occur each year, averaging one every five minutes. Currently, two-thirds of stroke survivors leave hospital with a disability, according to the Stroke Association.

→ **go.nature.com/2TQKCb9**

EPIDEMIOLOGY

REPEAT ANTIBIOTIC PRESCRIBING LINKED TO HIGHER HOSPITAL ADMISSIONS

Scientists have revealed an association between the number of prescriptions for antibiotics and a higher risk of hospital admissions.

The finding come from a study based on the data of two million patients from across England and Wales.

Patients who had nine or more antibiotic prescriptions for common infections in the previous three years are 2.26 times more likely to go to hospital with another infection in three or more months.

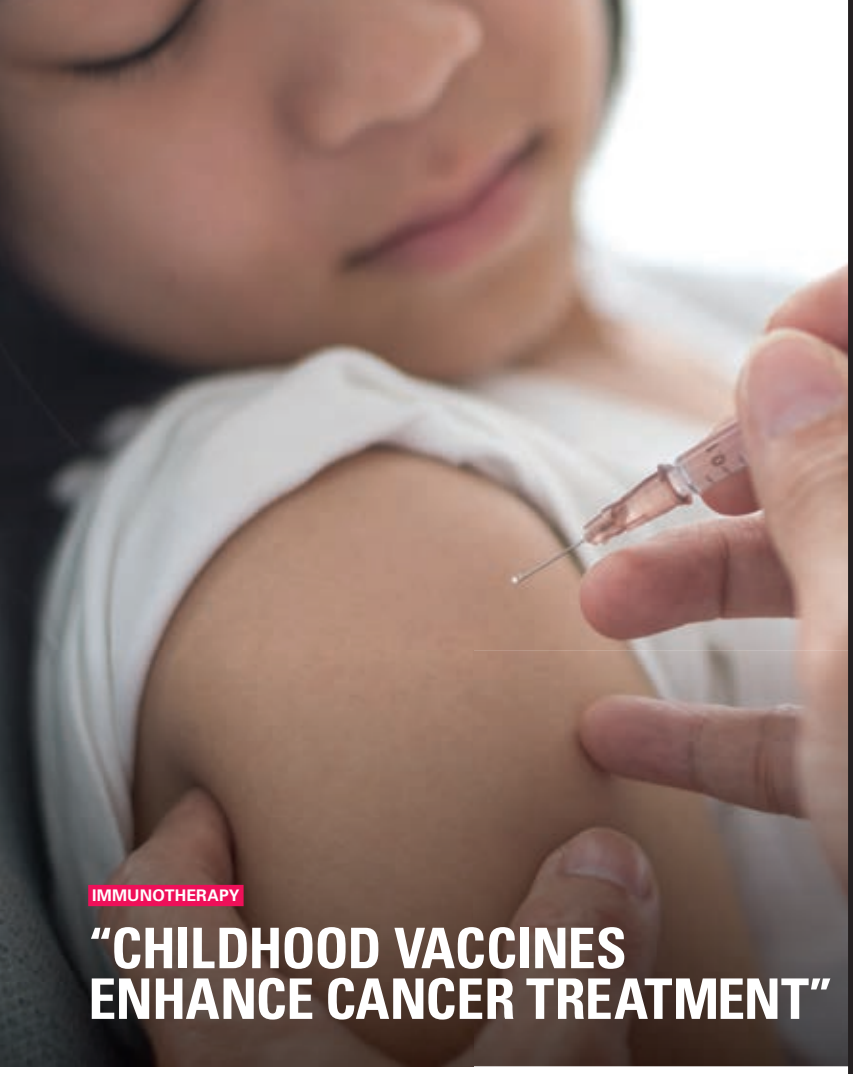
The patient records, from 2000 to 2016, covered common infections, such as upper respiratory tract, urinary tract, ear and chest infections and excluded long-term conditions, such as cystic fibrosis and chronic lung disease.

It is not clear why hospital admissions are linked to higher prescriptions. The team said more research is needed.

The risks of going to hospital with another infection were related to the number of the antibiotic prescriptions in the previous three years.

Those who had two antibiotic prescriptions were 1.23 times more likely, those who had three to four were 1.33 times more likely, and those who had five to eight were 1.77 times more likely to go to hospital with another infection.

→ **bit.ly/2TEaoRj**



IMMUNOTHERAPY

"CHILDHOOD VACCINES ENHANCE CANCER TREATMENT"

Scientists claim new research shows that pre-immunisation, acquired through common childhood vaccines, can be used to enhance therapeutic cancer treatment.

The University of Helsinki team discovered that when animals were pre-immunised with an ordinary vaccine (for example, anti-tetanus), engrafted with tumour and then treated with the new hybrid viral platform called PeptiCRAd, they showed a dramatic improvement in tumour-specific immune response.

As a consequence of this, there was significantly improved anti-tumour efficacy.

Research lead Professor Vincenzo Cerullo claimed this approach can be easily translated into clinical trials, as it relies on pre-existing immunity of vaccines included in the national vaccination programs worldwide.

He said: "This method has potential to have a significant impact on current immunotherapy protocols."

Due to the high coverage of international vaccination programmes, the majority of the worldwide population has been vaccinated against common pathogens, leading to a pathogen-specific immunological memory.

This is able to deploy a much faster and more effective immune response when we re-encounter the pathogens. This is called secondary response and it is stronger and faster than the first time we encounter a pathogen.

Generally speaking, the therapeutic cancer vaccines generate an anti-tumour response that is closer to a primary than a secondary immune response.

→ **bit.ly/2VWpsuV**

WHAT'S HOT AND WHAT'S NOT

HOT

SWEAT

A new sweat sensor that can detect cortisol levels in near real time may be used by NASA to study humans on deep-space missions.

HOT

CANNABIS

Researchers have identified an antibacterial compound made by cannabis plants that may serve as a lead for new drug development.

HOT

BILE

New bile acids have been identified that are not produced by our enzymes; they're made by microbes in the gut. This discovery will change how medical textbooks address digestion.

NOT

WIDOWHOOD

Widowhood accelerates cognitive decline among those at risk for Alzheimer's disease, according to a new paper.

NOT

BROAD-SPECTRUM ANTIBIOTICS

Doctors who use drugs that target antibiotic-resistant bacteria as a first-line defence against pneumonia should probably reconsider this approach, according to a new study.

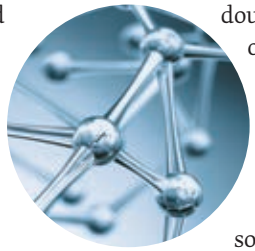
NOT

SWEET DRINKS

Drinking 12 ounces of sugary drink more than once per day is linked to higher levels of triglycerides, in middle -aged and older adults, both of which have been shown to increase risk of cardiovascular disease.

BIOCHEMISTRY

New molecules for fighting cancer



Cells can survive and multiply under more stress than previously thought, shows new research.

The discovery was made by inhibiting the essential gene DNA polymerase alpha, or POLA1, which initiates DNA replication during cell division.

The finding gives researchers new insights into DNA replication and may potentially be used for a new type of cancer treatment.

Research lead Professor Luis Toledo said: "If we are visionaries, I'd say we might be at the birth of a whole new set of molecules that could be used in fighting cancer.

"Basically, if we turn the finding on its head, this novel strategy aims at exploiting an in-built weakness in cancer cells and make them crash while they divide."

When a cell divides, the double DNA strand is opened lengthwise like an unzipped zipper. The new double strands are built at each of the separated strands, so you gradually get two new "zippers".

Before the new halves of the zipper are made, a bit of DNA is temporally exposed in single stranded form. This process is required for the new zippers to form.

Large amounts of single-stranded DNA have traditionally been considered to be a sign of pathological stress during cell proliferation.

The researchers discovered that DNA unzippers act more loosely than expected. This can generate large amounts of single-stranded DNA, which the researchers show is no more than a form of natural stress that cells can actually tolerate in high quantities.

→ **bit.ly/334okHl**

CELL BIOLOGY

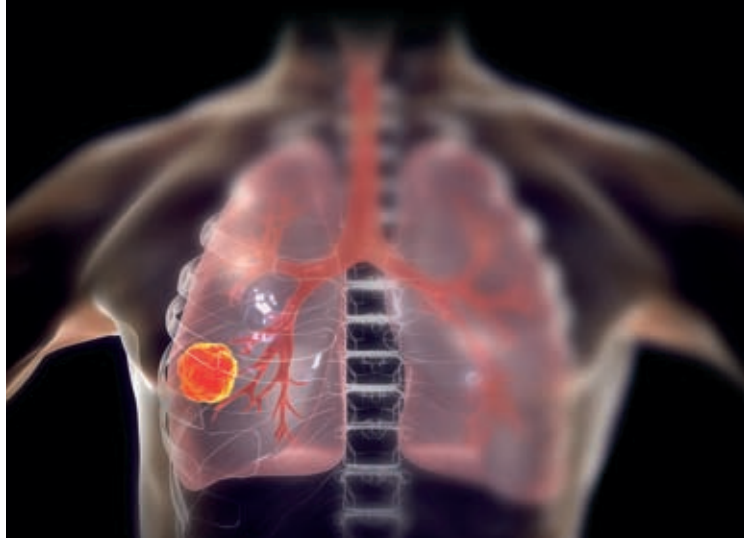
"CANCER CELLS HIBERNATE IN LUNGS"

Healthy lung cells support the survival of breast cancer cells, allowing them to hibernate in the lung before forming secondary tumours.

The claim comes from new research from the Francis Crick Institute.

The findings could help the development of new treatments that interfere with this behaviour, reducing the number of secondary cancers.

The study used a mouse model to show that, after cancer cells from a breast tumour arrive in the lungs, a signal sent out from the lung cells causes cancer cells to change shape and grow protrusions that latch onto the lung tissue. The



UNDER THE MICROSCOPE

This month: Gold

So, tell me about gold.
It is a chemical element with the symbol Au (from Latin the "aurum") and atomic number 79, making it one of the higher atomic number elements that occur naturally.

Tell me more.
It was also the title of one of Spandau Ballet's biggest hits, which reached number two in August 1983, but failed to knock KC and the Sunshine Band's smash hit "Give It Up" off the top spot.

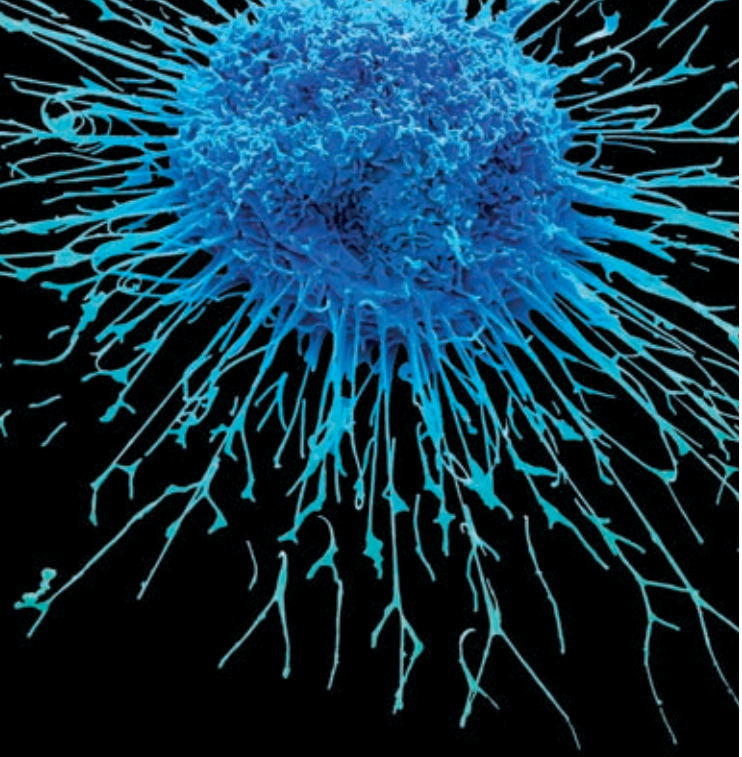
Haha. I was thinking less pop music and more science.
Sorry. A novel blood test has been developed that uses gold nanoparticles. It has been shown to identify extracellular vesicles (EVs), which are signals released by cancer cells. The development could result in earlier diagnosis and better treatment.

How do these EVs function?
They are being called the "next generation of potential biomarkers" in blood. EVs are nanoparticles that are constantly emitted by healthy cells and cancer cells to enable cell-to-cell communication. The cargo that they transport (DNA, proteins and other molecules) can reveal a lot about what is going on inside the cell.

What did the scientists do?
They used an electrically activated nano-fluidic chip that helps capture only cancer-emitted EVs and coupled this with a special type of gold nanoparticle attached to antibodies that stick to molecules found only on the surface of cancer EVs. The gold nanoparticles emit a unique signal when hit with laser light and this can be used to detect a patient-specific EV fingerprint.

What were the results like?
The technology, which was tested on blood samples from 23 melanoma patients, accurately detected cancer EVs in the blood samples, and successfully tracked how the cancer EV fingerprints changed.

IMAGES: ISTOCK/SCIENCE PHOTO LIBRARY



lung cells then protect them within the lung tissue.

By using a treatment that interferes with the growth of these protrusions on the breast cancer cells, the researchers found that mice which received the treatment grew fewer secondary tumours than the control mice.

They then analysed the genes that are turned on in the hibernating cells.

This enabled them to find a key gene, sFRP2, that regulates the formation of cell protrusions and the survival of breast cancer cells in the lung.

Erik Sahai, co-lead author, said: "Cancer can survive, hibernating in different parts of the body, for many years.

"Showing how the microenvironment around the cancer cell can support its survival (in our case how the lung cells help the breast cancer cells) opens the door to potential new treatments which target this relationship."

→ **go.nature.com/2TBE55t**

INCIDENT MANAGEMENT

STREPTOCOCCUS OUTBREAK

An outbreak of *Streptococcus* that killed 15 older people has been downgraded by the NHS after no new cases emerged for six months.

Some of the control measures that were put in place in mid and west Essex to stop the spread of the outbreak have now been lifted.

A total of 39 patients contracted group *A Streptococcus*, but the incident management team has now been disbanded. Mid Essex Clinical Commissioning Group (CCG) said it will "remain vigilant in the coming months".

The CCG added that it is "working closely with partners to monitor the situation and will continue to do so".

It has also commissioned an independent investigation into the outbreak, which is due to be published this spring.

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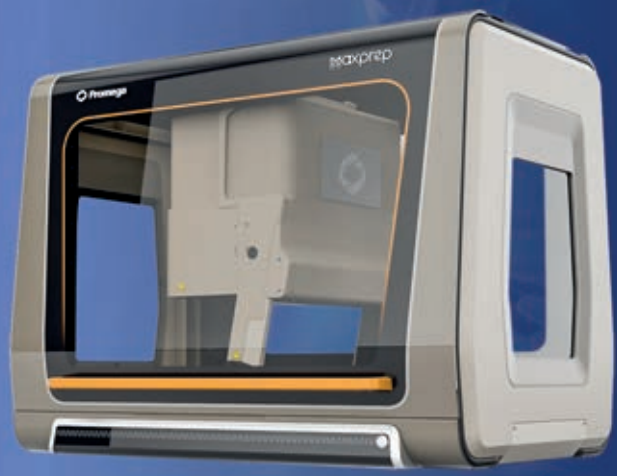

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TECH NEWS

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TECH TRANSFER

Technology and product development company TTP and DiaSorin, a global leader in the *in vitro* diagnostic (IVD) field, have signed an exclusive licence and technology transfer agreement.

DiaSorin will combine its extensive molecular test offering with TTP's Puckdx platform to develop a single-use, sample-to-answer, molecular diagnostics point-of-care platform for human IVD applications.

→ **ttpcom**
diasorincom

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PHARMACOGENOMICS

Pharmacogenomics is a new and developing research field focused on the interplay between the human genome and the safety and efficacy of modern drugs, which may level the playing field for patients.

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FLUIDIC ANALYTICS

PROTEIN LABELLING

Fluidic Analytics Ltd has launched a time-saving and affordable protein labelling kit – fluidiphore rapid amine 503.

Absorbing at 503nm, the new kit can be used with a multitude of techniques, including the company's groundbreaking Fluidity One-W instrument for protein interaction analysis.

Fluorescent labelling of proteins, such as antibodies, DNA and lipids, is widely used to investigate and better understand protein structure and function.

→ **fluidiccom**

THE BIG QUESTION

THIS MONTH WE ASK

"What could labs do to be more environmentally sound?"

Kip Heath

Deputy Trust Lead Healthcare Scientist
Great Ormond Street Hospital

The NHS is responsible for 5.4% of the UK's carbon emissions and produces 1% of all UK waste. I strongly believe that all NHS staff, including us as biomedical scientists, have a responsibility to reduce our impact on the environment. We are here to help maintain the health of the population, and what better way to do that than make sure that life on earth will still be viable for generations to come?

The best way labs can become environmentally sound is to collaborate and share best practice. University College London has developed the Laboratory Efficiency Assessment Framework. The pilot covered 103 laboratory groups from 16 institutions who, in total, saved 620 tonnes of CO_2 and £400,000, proving that environmental sustainability can be financially beneficial as well, at which point, who can argue against it?

I would love to see biomedical scientists (led by the IBMS) across the country engaging with this process championing sustainability within the NHS in order to benefit staff and patients.

Some other quick ideas that would improve the carbon footprint of a laboratory include: defrosting freezers to make them more energy efficient; ensuring computers and lights are switched off at the end of the day; stopping printing unnecessarily; switching to recycled (non-bleached) paper; considering if documents and letters can be sent electronically, rather than posting; asking suppliers what they are doing to reduce their carbon footprint.

IMAGE: GETTY

Karen Brazier

Technical Services Manager, Biochemistry
NHS Greater Glasgow and Clyde

A Green Future is the 25-year environment plan set out by our government. It aims to deliver cleaner air and water across the country, as well as protecting wildlife habitats and at-risk species.

As healthcare workers, we also have a responsibility to contribute towards these goals, without compromising on the quality of our service and patient care.

With increasing demands on our time and service, environmental concerns are often pushed down the list of priorities, but developing a more environmentally sound approach is worth considering and would also bring additional benefits to our organisations.

Plastic waste from laboratories is considerable – an article in the journal *Nature* from 2015 estimated that laboratory waste totalled 5.5 million metric tonnes in 2014. There are some systems available now that claim to reduce single-use plastic sample bags by using reusable transport racks directly from the point of collection to the laboratory. This is supported by a trial carried out by a hospital laboratory in Cornwall that reduced their use of sample bags by 75%. Clearly there needs to be an initial investment by the health board or trust.

We are not exempt from considering the environment in our laboratory practice just because we work for the NHS. We have a responsibility to keep environmental impact near the top of our priorities and be creative in our approach to finding solutions to reduce waste and carbon footprint wherever possible.

Cherie Beckett

Biomedical Scientist, Microbiology
Princess Alexandra Hospital
NHS Trust, Harlow, Essex

Being environmentally sound at home can include cutting down on single-use plastics or committing to recycling more, but how can we mimic this in the laboratory? At home, a quick rinse of suitable plastics before recycling is sufficient. In the laboratory, many consumables are contaminated by biohazardous waste and destined for a clinical-waste stream or autoclaving only.

Historically, many microbiology laboratories used metal loops to inoculate agar plates, which would then be "flamed" to sterilise between use, but with sample numbers ever increasing, this is not always practical and thus, disposable single-use only plastic loops are more common. We need to think more laterally. We could consider working with companies who are more environmentally aware. This might include receiving consumable deliveries in reusable crates that are then returned to the supplier. Also, it is so frustrating to receive small reagent kits in large cardboard boxes with an enormous amount of foam-padding inside, which cannot be recycled.

Other thoughts include reducing specimen transport bags, but this would need some thought to safely balance infection control, or reducing aliquoting samples into secondary receptacles and testing/storing more routinely in the primary tube. Much work is still to be done in this area and laboratories would benefit from in-house environmental ambassadors to pave the way for change.

OMEGA-3 FATS MAJOR REVIEWS MINOR EFFECTS

Lee Hooper takes us behind the headlines to look at the findings of two systematic evidence reviews of the benefits of omega-3 fats.

In the world of dietary healthcare, omega-3 fats have a solid reputation for their protective and enriching qualities. Derived from fatty fish, nuts, seeds and a few other sources, they are said to offer defence against a range of conditions, including heart disease, cancer and stroke. As a result, but also because the western diet has tended to move away from the natural sources of these fats, omega-3 supplements have become big business – the worldwide market was worth $33bn in 2016 and projected to hit $57bn by 2025.

However, the accepted wisdom of the benefits of omega-3 fats has been thrown into doubt with the publication of the two new systematic evidence reviews. The first, published in the *British Journal of Cancer*, has found that omega-3 and omega-6 fats and total dietary polyunsaturated fat have little or no effect on cancer diagnosis and death rates, and may even raise the risk of prostate cancer slightly. The second study, in the *Cochrane Database of Systemic Reviews*, revealed that the key omega-3 fats (EPA and DHA from fish, and ALA from plants) also have little effect on heart disease diagnoses and deaths – any positive impact is small.

Best evidence

Both reviews were conducted by a team of researchers drawn largely from Norwich Medical School at the University of East Anglia and were headed up by Lee Hooper, a Reader in Research Synthesis and Nutrition.

The impetus for the reviews came from the World Health Organization (WHO): "The question was posed for us by WHO as they want to update their guidelines on polyunsaturated fat, including omega-3s and omega-6s," says Hooper. "So they naturally wanted to know what the best evidence is on the health effects of all those across a wide range of outcomes."

The two papers just published are part of a series of reviews looking at the effects of these fats on all sorts of conditions, with diabetes and depression among them. "Our research question came about because they are keen to know whether they should be encouraging people to eat more omega-3s and polyunsaturated fat in general," says Hooper. "In trying to address their question we embarked on a rather longer adventure than expected."

The research teams started work on the reviews in 2016 with a trawl of the various databases. "We pulled in trials from as far back as the 1960s. I think those are probably the oldest," says Hooper. "The late 1950s and early 1960s were when people started to look at fats and health in some detail and they ran some really good trials at that time. Plenty of other trials have been carried out every decade since." The most recent trial included in the reviews was published in July 2019. In all, they looked at 86 randomised control trials (162,796 participants in all) for the heart disease review, and 47 (108,194 participants) for the cancer review.

In delivering omega-3 and other fats to the participants, most of the trials used supplements. "It's just much easier to do that than to encourage people to eat more oily fish," says Hooper. "Of course, we were interested in oily fish trials too, and we pulled them in where we could, but there just aren't many of them. So the evidence relates more to omega-3 supplements because that's what was largely given during most of the trials."

Not delivering

Could the results reflect some key difference between the supplements and the natural sources? "Not that we are aware of," says Hooper. "There is nothing

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- ✔ **1989-1999**, Heart Health Dietitian, Shropshire,
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IMAGES: ISTOCK

specific about the supplements. They come in many different forms. Some early trials gave straight oil – people had to drink it, which sounds pretty grim. But there is not a consistent coating, for example, that you could say is a potential issue. In some trials the oil was concentrated and is some it was enriched, but the effects are remarkably consistent in that we don't see many effects. And even when we do, they are very small. So I don't think it's the supplements that are the issue. It's that omega-3 itself is not delivering what it is believed to deliver."

This hasn't come as a huge shock to Hooper, who conducted an earlier systematic review as part of her PhD. "I was surprised then that we saw little effect of omega-3 on cardiovascular outcomes. I was advising people to eat lots of omega-3 because I was convinced they were doing good. Recent large and long-running trials have added a lot of information, but the results still look consistently unhelpful. They have shown us there is a beneficial effect, but such a small one."

"Recent large and long-running trials have shown us there is a beneficial effect, but such a small one"

Small effect

What might WHO make of this? "They will look at the evidence in its entirety, including our evidence, possibly balancing it with the evidence from cohort studies. They are also looking at data for pregnant women and children. All of that will come together when they bring out their advice."

In the meantime where does that leave dietary advice? "The advice to eat at least two portions of fish a week, one of which is oily, is still good. Oily fish has lots of healthy stuff in it besides omega-3. It's a good source of protein, selenium, iodine and calcium and so on. But I think taking a supplement is another matter. They do bring triglycerides down, but what they don't seem to do is provide much protection from cancer or heart disease. It's a small effect for something that can cost people a lot of money. They might be better off spending it on something that might be better for them – such as pair of running shoes!" BMS

40 calories

LAUGHTER BURNS CALORIES

A STUDY FOUND THAT LAUGHING FOR 10 TO 15 MINUTES A DAY CAN BURN APPROXIMATELY 40 CALORIES.

EXPRESSIONS OF EMOTION

THE SCIENCE OF LAUGHTER

Sophie Scott, Professor of Cognitive Neuroscience at University College London, asks why we laugh, what it means and argues that it's time to take laughter more seriously.

Laughter is something that humans closely associate with jokes and comedy. In fact, the late psychologist Robert Provine found if you ask people about what makes them laugh they talk about humorous materials like TV shows and comedians. However, Provine also found that if instead of asking people what makes them laugh, you simply watch them out and about and note when they laugh, then it quickly becomes apparent that laughter is primarily a social behaviour. We laugh when we are with other people. Provine found that we are 30 times more likely to laugh when we are with other people than when we are on our own. And most of the time we are not laughing at jokes and comedy – people laugh to make and maintain social bonds, to show agreement, affiliation, understanding and recollection. Indeed adult humans use laughter in incredibly nuanced ways – we will use laughter to try and manipulate or manage social situations, and we will use laughter to mask other emotions – like fear or sadness – which we may be trying to actively mask.

What is laughter?

Laughter is a non-verbal expression of emotion, and that means that it is highly unlike speech or song. In fact, it is more

like an animal call than it is like speech, and it shares this characteristic with other non-verbal expressions of emotion, like screams or sobs.

We produce laughter largely at the rib cage, where large, fast contractions of the intercostal push air through the vocal tract at high pressure. The repeated contractions lead to each individual "ha" burst of the laughter, and if the contractions run into each other, the laughter becomes a longer noisy spasm. The pressures generated – especially when people laugh helplessly – can be much higher than those generated during speech or song, and consequently some very strange noises can be generated. Certainly when I laugh hard, I have a very high-pitched laugh, far higher than I could sing.

Laughter is thus a relatively primitive, simple way of making a sound – which is consistent with the fact that, along with crying, we can produce laughter from a very early age. Crying – for attention, food, pain, sleep – is critically important for human babies and they can produce this vocalisation from early in life. The next vocalisation – normally appearing after smiling (at around six weeks) – is laughter, which babies start to produce at around two to three months. Initially, babies laugh highly reactively – at being tickled, or games of peekaboo – but note that this is also a highly social behaviour. We cannot tickle ourselves – someone else needs to touch us, and peekaboo requires another active agent looking at us. Thus right from the beginning of our lives, laughter is an expression elicited in a social context. Quickly, this becomes even more complex. By the time they are around 12-15 months old, babies' understanding of laughter is pretty nuanced; they will use the presence of parental laughter to decide if situations are dangerous or not, and they will also do things to make their parents laugh. And we then continue to learn about laughter until we find the highly complex pattern of adult human laughter that Provine described.

Like human babies, laughter in apes and rats is seen first when babies are tickled by parents

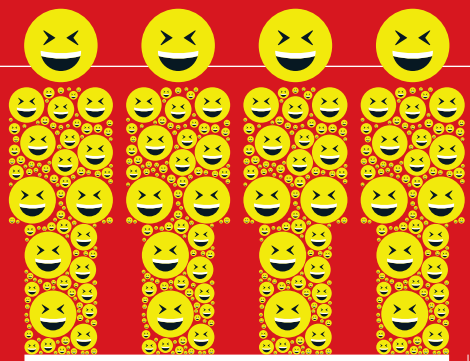
Apes and rats

Strikingly, however, laughter is not a behaviour that is limited to humans. Laughter has been well described in other apes – indeed, Darwin wrote a lot about laughter – and a laugh-like vocalisation has even been described in rats. Laughter in apes is relatively similar to human laughter, though rat laughter is a high frequency chirp. Like human babies, laughter in apes and rats is seen first when babies are tickled by parents (notably, only human babies laugh at peekaboo, which may be an example of some more profound differences between humans and other mammals). As apes, rats and human babies grow older, laughter becomes associated with play behaviour. Indeed, Panksepp, who did many wonderful studies of rat laughter, said that across nature, the most common role for laughter was as an "invitation to play".

Play is a critically important family of behaviours, which is found across all mammals when they are juveniles, and some mammals play all their lives. I suspect, therefore, that there may be more examples of laughter out there in the world of mammals, if it really does play an important role in demonstrating playful intent.

Behavioural contagion

In terms of the neural basis of laughter, we have data implicating both the supplementary motor area and the hypothalamus in the generation of laughter, but it is also likely that lateral motor fields are involved in the generation of more communicative



laughter, such as that which occurs in conversational speech. This is hard to test, as it is extremely difficult to get people to laugh under normal laboratory conditions. It's a lot easier to look at brain responses to hearing laughter. Using functional magnetic resonance imaging, we have found that, compared with hearing emotional vocal expressions connoting fear and disgust, hearing laughter induces activity in orofacial mirror regions.

These are brain regions that are activated both by hearing laughter, and by moving your face into a smile. We interpreted this as associated with the ways that laughter can be behaviourally contagious – when we hear someone else laughing, we often join in, even if we have no idea why they are laughing. This behavioural contagion is intriguing because it's not limited to laughter – the same thing can happen with yawning and coughing – and because it remains highly social. We are much more likely to catch a laugh from someone we know than someone we do not know. Indeed, we learn to catch behaviour in this contagious way. Adults laugh when babies laugh, but babies do not catch laughs from their parents until they are much older. More research is needed, but it is clear that this contagious laughter is something we learn to do. And it can go wrong. Teenage boys at risk of psychopathy find laugher less contagious than normally developing boys, and their brain shows a significantly smaller priming response.

Difficult to ignore

Using perceptual studies of how the brain responds to laughter, we have also found that the distinctions between spontaneous laughter and more communicative laughter can be seen – when people hear the sounds of someone laughing completely helplessly, we see lots of auditory activation, possibly because of the very unusual sounds produced. When people hear a more controlled, communicative laugh we get lots more activation in medial prefrontal fields associated with mentalisation processes – i.e. working out what someone else is thinking. When we hear someone laughing we are trying to work out why and what it means. Laughter is never neutral. Indeed, we have recently found that simply adding laughter onto the end of a joke makes people rate the joke as funnier. Laughter can be extremely difficult to ignore.

There is vanishingly little scientific research into laughter and it's probably essential to extend this very limited set of studies, as laughter may be one of the more important social behaviours in which we engage. A set of studies from the US has shown that couples who deal with stress by sharing positive emotions (mostly sharing smiles and laughter) not only get less stressed straight away, but they are happier in their relationships and stay together for longer. It's not because laughter is a bit of magic dust that makes everything better – the presence and use of the laughter is an index of how close and strong that relationship is. Recently studies from the same lab have even shown that – compared with couples who react to stress with negative emotions, or by suppressing emotions – couples who face a difficult situation with smiles and laughter are healthier. Using laughter to deal with stress not only works, but maybe it's actually good for you. Sounds funny, but maybe it's time to take our laughter a little more seriously. BMS

LAUGHTER IN RESEARCH

It has been more than 40 years since Norman Cousins published an article in the *New England Journal of Medicine* extolling the potential medicinal benefits of laughter and humour.

Laughter burns calories. One study found that laughing for 10 to 15 minutes a day can burn approximately 40 calories – which could be enough to lose three or four pounds over the course of a year.

A study from Norway found that people with a strong sense of humour outlived those who don't laugh as much. The difference was particularly notable for those battling cancer, the researchers reported.

Laughter can affect pain perception. In one study 200 subjects were subjected to a painful cold-pressor stimulus after being shown a film. Those who viewed a humorous film had a significant advantage in pain tolerance time after a 30-minute wait period.

The cardiovascular effects of laughter appear to be quantifiable, although potentially short-lived. A study of 10 healthy subjects showed that cardiac parasympathetic activity decreased immediately on watching a comedy video, and just as quickly returned to baseline when finished.

The SMILE study reported a 20% reduction in agitation for those with dementia using humour therapy.

Professor Scott's research summary

"I am interested in the neural basis of vocal communication – how our brains process the information in speech and voices, and how our brains control the production of our voice. Within this, I am interested in the roles of streams of processing in auditory cortex, hemispheric asymmetries, and the interaction of speech processing with attentional and working memory factors. I am also interested in the expression of emotion in the voice. Finally, I am interested in individual differences in speech perception, and plasticity in speech perception, since these are important factors for people with cochlear implants."

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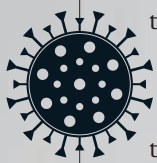
ACCREDITING HEALTHCARE

Ben Courtney, Head of Healthcare at UKAS, gives an update with the latest news from the service.

At the time of writing, only six months have passed since IBMS Congress and yet there has been much change at UKAS. We have continued to work with stakeholders, from collaborating with the European Federation for Immunogenetics (EFI) to ensure ISO 15189:2012 will meet EFI requirements to on-going plans with NHS England, NHS Improvement and Public Health England to ensure suitable testing can be included in scope to assure the quality of testing during the current COVID-19 outbreak.



As UKAS expands, we continue to be committed to improving our levels of customer service, as well as training opportunities for laboratory staff. Having completed the transition to ISO 15189:2012 from CPA Standards 18 months ago, UKAS is very aware of the need to improve the service that we provide to our customers. This is now formally measured and there are multiple initiatives in place aimed at continual improvement, including improved tracking of turnaround times, 12-month forward booking, further guidance on applying for extensions to scope and assessor resource analysis to limit the delay to assessment planning and booking in the future.

Healthcare accreditation is a key area of UKAS' expansion and, aside from the accreditation of medical laboratories, UKAS also accredits physiological sciences (IQIPS), imaging services (QSI), and point-of-care testing (POCT) under ISO 15189:2012 and ISO 22870:2016 and, of course, our medical EQA Providers to ISO/IEC 17043:2010.

I lead each of these areas now under a merged single healthcare section, the objective of which is to align accreditation processes, introduce efficiencies of assessment and ensure improved customer service, this being at an interesting time for accreditation in healthcare, with the revision of ISO 15189:2012.

ISO 15189:2012 revision

Work on revision to the medical laboratories standard ISO 15189:2012 has moved on significantly since the September IBMS Congress. International Standards are written by specific working groups within committees and these groups meet twice a year face-to-face, supported by remote video conferencing in between. Prior to the last face-to-face in Mexico in November, a working draft had been developed. However, thanks to my colleague and Head of UK Delegation, David Ricketts (representing the IBMS), we have moved on to committee draft stage. This is currently out for comment and a vote will be held prior to the next face-to-face meeting in April.

The estimated publication date of the final standard is the end of 2021 (possibly very early 2022) and the standard will be closely aligned in terms of structure and basic content to the general laboratories standard ISO/IEC 17025:2017. The impact this has on accreditation is that this will trigger another transition period, but it must be stressed that it will not be a transition as challenging as that from CPA Standards to ISO 15189:2012. Laboratories should be assured that the key requirements will already be met, that there will be a clear transition plan from UKAS and that the transition period will be three years. It is likely that in the first year UKAS delivers training webinars, and laboratories will have the opportunity to review and resolve any gaps. In year two, an assessment to the new standard will take place, regardless as to whether this falls in a laboratory's surveillance or reassessment year. In year three, plenty of time will be allowed to clear up any extra visits and associated decision-making. Awareness on the potential new requirements and the focus of the new version of ISO 15189 will be introduced to presentations from summer this year.

Training opportunities

Given the expansion of UKAS, we have recruited a new Commercial Director, Mark Bohun, in the last 12 months. Mark is supported by a new sales and marketing team, which is working closely on the needs and requirements of UKAS, but also our customer base. Over the next 12 months we will be increasing the scope and quantity of training courses and webinars to support professional development and increase awareness of requirements.

UKAS provides the assessor training

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course free of charge to anybody who applies to become a technical assessor (whether in full-time employment or a self-employed/retired individual).

We currently have vacancies for assessors in all medical laboratory disciplines, but also full-time Assessment Manager posts. Please contact me at ben.courtney@ukas.com for details.

Restructure at UKAS

In addition to sales, marketing and training changes, the UKAS Executive has reviewed the structure of the whole company over the last year. The medical laboratories section has now merged with IQIPS and QSI to form one operational healthcare section. This allows a closer calibration of assessment consistency between the various healthcare accreditation schemes. In turn, this opens up possibilities in working towards harmonisation of accreditation and potentially "joined-up" assessments – assessments led by a single Assessment Manager with a team that has the technical competence to look at all areas. This potentially reduces the effort overhead and improves efficiency of assessment visits, in turn bringing potential economies of scale for multi-scheme accredited laboratories.

The new structure also ensures closer work with our development colleagues in UKAS. Within the last six months we have accredited our first organisations under the new Medical Physics and Clinical Engineering (MPACE) scheme to BS 70000, which is based on ISO 15189:2012. Key development work over the next 12 months is the accreditation of biobanks and point-of-care testing (POCT).

POCT

As part of the revision of ISO 15189:2012, it is likely that POCT requirements will be included within the document as a normative annex to the revised standard. As third party assurance has been demonstrably proven to reduce risk, it is beneficial to both providers and patients of POCT if POCT is covered in the scope of an organisation's accreditation. Over the next 12 months, UKAS will be reviewing and providing guidance as to how customers can include this in a sustainable and a manageable way.

ISO/IEC 17011:2017 (the standard that UKAS must meet as a competent accreditation body) now provides more scope for UKAS to assess based on risk. It is expected that estimates for assessment for such work will be lower in assessment effort and lower in cost. For information on how to apply, organisations are encouraged to contact their Assessment Manager to establish what is required.

Collaborating

A key issue for laboratories has often been that with various assessments and inspections, the annual time and cost overhead has been high. UKAS continues to work hard with both regulators and other organisations providing assurance to reduce this burden.

For some years now, UKAS has been collaborating with PHE to cover the PHE requirements for antenatal and newborn screening and this continues to develop. Mechanisms to report back to PHE on both the outcome of assessments and notification on the assessments due continue to be improved and developed to ensure customers experience the benefit of this collaboration. Similar work is starting with the EFI. This is at a very early stage as ISO 15189:2012 requirements have only recently been mapped to EFI requirements. However, sharing of resources and observation of visits is the next stage of the process with a view to piloting UKAS assessments to ensure coverage of EFI requirements. BMS

Ben Courtney features on the latest IBMS podcast, discussing UKAS and accreditation. To listen, visit **ibms.org/resources/podcasts**

SUMMARY

Feedback from UKAS customers tells an important story – assessments are thorough, there is a high degree of confidence in the technical knowledge and expertise of our teams and the reports are accurate.

It also informs UKAS about customer frustrations regarding communication, the consistency between assessors and the turnaround times associated with decisions, evidence and the reports.

Developments in accreditation are important to ensure UKAS continues to meet the needs of stakeholders and the changing face of pathology. This is the driving force behind the initiatives above and it reinforces the need for UKAS to continue to deliver a high standard of service and add value to customers through assessments.

Customer satisfaction has improved significantly in the last 12 months due to UKAS' focus on four key areas: assessor consistency at assessor workshops, the issuing of guidance for extensions to scope, presentations on the management of a flexible scope of accreditation and the drive to reduce the decision-making backlog. UKAS is not resting on its laurels and further improvements are required. For the 2020-21 financial year, increased tracking of improvement action and assessment report turnaround time will be in place and a more streamlined approach to handling extensions to scope will be introduced. Assessment Managers will be encouraged to ring-fence time with laboratories to ensure UKAS is prepared and sufficiently agile to adapt to any changes in accreditation due to pathology networks.

The objective over the next year is to ensure satisfaction improves and that laboratories derive the maximum possible benefits from accreditation. Whether that is introducing a new extension to scope, POCT accreditation or avoiding the prospect of a gap in accreditation during periods of change, regular contact with your Assessment Manager is key.

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HEALTH AND WEALTH IN THE RENAISSANCE

Stephen Mortlock looks back over health and wellbeing in the period of transition from the Middle Ages to modernity.

Between the 14th and 16th centuries there was a rediscovery of classical philosophy, literature, science and art: this was the Renaissance (rebirth).

A global exploration opened up new lands and cultures to European commerce, which then led to the emergence of prosperous cities and a wealthy merchant class, especially in Italy.

This Italian Renaissance started in Florence, a city which already had a rich cultural history, but now wealthy citizens could become patrons to the arts and science. Some of the greatest thinkers, authors, statesmen, scientists and artists in human history thrived during this era; artists like Da Vinci, Botticelli and Michelangelo were all born in Florence.

This period also saw the development of a modern commercial infrastructure, with an international banking system, a systematised foreign exchange market, insurance, and ultimately government debt. The Italian cities acted as the main hubs for international trade in commodities such as wool, cloth, silk, spices, silver and armour. The merchants wanted to show off their wealth and furnished their homes with the most modern art, furniture and books, created either by local artisans or from further afield. In 1450, the invention of the moveable-type printing press by Johannes Gutenberg allowed little-known texts from early humanist authors (Francesco Petrarch and Giovanni Boccaccio) to be printed and distributed to the masses and their ideas spread quickly throughout Europe. Venice became dominant in the production of printed books.

The Renaissance was a unique time when the fields of art, architecture and science fused together. Art became characterised by realism and naturalism, while artists strived to depict people and objects in a true-to-life way using perspective, shadows and light to add depth to their work.

Leonardo da Vinci incorporated scientific principles, such as anatomy, into his work, so he could recreate the human body with extraordinary precision. Filippo Brunelleschi (1377–1446) studied mathematics to accurately engineer and design immense buildings with expansive domes, such as those found on the Cathedral of Santa Maria del Fiore. Scientific discoveries led to major shifts in thinking: Galileo and Descartes presented a new view of astrology and mathematics, while Copernicus (1473–1543) proposed that the Sun, not the Earth, was the centre of the solar system. The protestant movement under Martin Luther (1483–1546) was attacking the Catholic clergy and, thanks to the printing press, "95 Theses" (originally posted on the door of a church in Wittenberg in 1517) and other writings began to influence more and more European people. In 1534, he published a complete translation of the Bible into German, underlining his belief that people should be able to read it in their own language. The translation contributed significantly to the spread and development of the German language. Renaissance style and ideas, however, were slow to reach England, and the Elizabethan era in the second half of the 16th century is usually regarded as the height of the English Renaissance, with the beginning taken to be 1485, when the Battle of Bosworth Field ended the Wars of the Roses and inaugurated the Tudor dynasty.

Alongside this was a medical Renaissance, where great medical personalities and scholar humanists made unique advances to medicine and surgery. The foundations of surgery as we know it in theory were laid during the Renaissance by the anatomists who robbed graves to obtain bodies for study.

Medical Renaissance

The city and University of Padua have a long tradition and a great reputation in anatomic studies, dating from the founding of the university in the year 1222. During the second half of the 15th century, the flourishing trade and cultural, social, and political life of Venice attracted a great number of scientists and students from all over Europe who contributed to the establishment of Padua as an international centre for culture and the sciences. Andreas Vesalius (1514–1564) was Professor of Surgery and published a fully illustrated description of human anatomy called *The Fabric of the Human Body* (1543), and although he based much of his work on the ideas of Galen, by dissecting executed criminals, he was also able to show some discrepancies; the human jaw bone was made from one bone, not two and the breastbone had three parts, not seven, as had originally been theorised.

"The foundations of surgery as we know it in theory were laid during the Renaissance"

Towards the end of the Renaissance and beginning of the modern era, William Harvey (1578–1657), the noted British medical doctor and cardiovascular researcher, published his findings showing detailed anatomy and physiology of the circulatory system in *The Motu Cordis* (1628). Although his work was extensive it was not quite complete, because he was unable to show visual evidence of a link between the minute final terminations and initial branches of the arterial and venous systems. It was Malpighi (1628–1694) who provided the missing link with his work on capillaries using the new "microscope".

Giovanni Battista Morgagni (1682–1771) conducted extensive diagnostic sessions with patients as well as postmortem examinations of over 700 cases, as he tried to interpret the underlying anatomical lesions from the diseases the patient had suffered. His 1761 book *De Sedibus et Causis Morborum per Anatomen Indagatis (The Seats and Causes of Diseases Investigated by Anatomy)* contained the results of 60 years of scientific work.

Further afield, Franciscus Sylvius (1614–1672) was a professor of medicine at the University of Leiden (1658–72). He was a physician, physiologist, anatomist and

chemist who developed the 17th-century iatrochemical school of medicine, which held that all phenomena of life and disease are based on chemical action. According to the legend, Dr Sylvius created the first iteration of genever (the forefather of gin) when researching a cure for stomach and kidney disorders. There is certainly evidence to suggest that he was distilling medicines with botanicals, such as juniper berry oil, and, allegedly, the demand was so great for his cure that he went to local distillers who helped him make it in larger volumes and the rest is history. Except it is probably wrong as although some of his papers make reference to juniper berries, blood circulation and academic theories, there is no mention any of mass distillation, nor do they ever refer to genever.

Diseases

Every generation in European history between 1350 and 1720 seemed to endure outbreaks of the Black Death and in 1510 Europe was still recovering from massive depopulation caused by an outbreak in the 1340s and struggling with a less fatal but still horrifying epidemic of syphilis. Then, in July and August of that year, people became stricken with a respiratory illness described as a "gasping oppression" with cough, fever, and a sensation of constriction of the heart and lungs. Said to have first arisen in Asia, the disease spread to almost every part of the known world (except the New World).

It arrived in Sicily and Italy along trade routes from Africa and quickly spread throughout Europe. The pandemic was well documented by people who lived through it and wrote about it after the event. These books became available to scholars and the general public, including physician John Caius (1510–1573), surgeon Ambroise Paré (1510–1590) and historian Jean Bouchet (1476–1557). Fortunately, the infection burned out soon after it started. Among the people who contracted the illness was the eight-year-old future Pope Gregory XIII (1502–1585) who became dangerously ill with the disease but fully recovered.

The sixteenth-century epidemiologist Guillaume de Baillou (1538–1616) did extensive studies of the epidemics that plagued Paris, and is credited with providing the first clinical description of "whooping cough" in 1578. His descriptions of plague (which killed about 30,000 people in Paris in 1580), diphtheria, and measles and other works on epidemiology, were described in *Epidemiorum (Of Epidemics)* (1640). His work influenced later scholars including the great 17th-century Hippocratic physician Thomas Sydenham (1624–1689). In 1679, Sydenham, a devout Parliamentarian during the English Civil War, gave whooping cough the name "pertussis", meaning a violent cough of any type. He was among the first to describe scarlet fever, differentiating it from measles. In his 1676 *Observationes Medicae* he also described malaria and how "anyone dwelling in the locality of marshes and lakes became impressed with a certain miasma which produces a quartan ague".

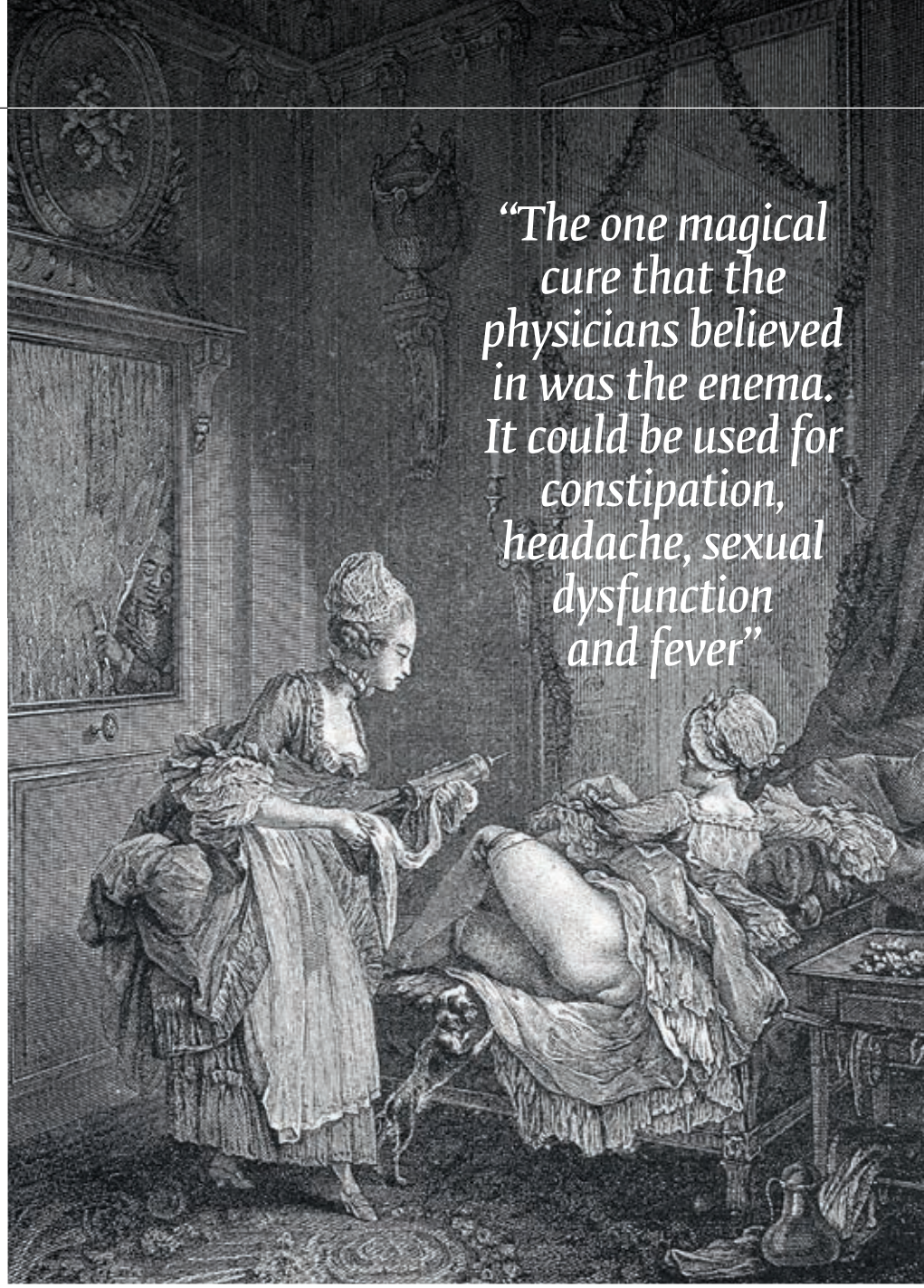
Treatments

As with all periods of history, home remedies were often handed down through generations from mother to daughter. Girls learned how to mix up remedies using natural ingredients such as honey and local herbs, for family and friends. But now more people were writing them down because more people could now read and write. The increasing literacy of the population and the fact that they were published in a familiar language, no longer Greek and Latin, made herbal books a great success for the publishers. With their detailed descriptions and their medicinal information they became the predecessors of pharmacopoeias and science books. The English botanist William Cole (1626–1666), wrote that "the mercy of God... maketh... Herbes for the use of men, and hath... given them particular signatures, whereby a man may read... the use of them". The daisy-like Euphrasia flower (or "eyebright"), for example, was used in various concoctions for treating the eyes through the 17th century.

European travels to America and Asia led to the arrival of new ingredients for medicines. Rhubarb from Asia was widely used to purge the bowels. The bark of the cinchona tree (quinine) was imported from South America because of its effectiveness in treating fevers, especially malaria. Opium was imported from Turkey and used as an anaesthetic amongst other things. Tobacco was initially promoted as a cure-all when it arrived from America, being recommended for toothache, poisoned wounds, joint pains and as protection from plague.

The one magical cure that the physicians believed in was the enema. It could be used for constipation, bowel management, headache, sexual dysfunction, asthma, allergy, and fever. Although the enema had been around for a long time, it gained more popularity in the Renaissance era. The French monarch Louis XIV (1638–1715) was fond of this therapy and

IMAGES: ALAMY/ISTOCK



"The one magical cure that the physicians believed in was the enema. It could be used for constipation, headache, sexual dysfunction and fever"

practised it daily. Taking cues from a similar Native American tradition, Western healers also made a habit of performing tobacco-smoke enemas for respiratory conditions, while they preferred liquid tobacco enemas for treating hernias. And on the subject of enemas, smoke was not the only thing being introduced to Renaissance rectums in the name of good health. As an effective method of getting medicine in the body and targeting intestinal issues, the enema was central to the era's medical arsenal and was considered appropriate treatment for everything from constipation to cancer.

Following a tobacco enema, what better than an emetic to induce vomiting to help remove more perceived excesses from the body, be it snake venom or over-indulgence of alcohol or an illness brought on by a misalignment of the planets? Leonardo Fioravanti (1517–1588) encouraged the use of emetics and tended to prescribe these as a first course of action for almost every ailment. He collected together an imposing armoury of purgatives and emetics, some based around the genus *Helleborus* (black hellebores), but also included white hellebores or veratum (in the family Melanthiaceae), metallic antinomy and mercury. He labelled these with half-scientific and half-religious names: "angelic electuary", "magistral syrup", "blessed oil" and his favourite "fragrant goddess". Another devotee of the curative nature of emetics was Tomasso Bovio (1521–1609) whose concoction "Hercules" was reputed to have caused the patient to "vomit a catarrh as big as a goose liver".

With the emergence and spread of syphilis throughout the Western world, there was a need for a treatment. In the early 16th century, treatments for syphilis included guaiacum (or holy wood) and sweat baths as it was thought these induced salivation and sweating, which helped to eliminate the syphilitic poisons. Paracelsus (born Philippus von Hohenheim, 1493–1541) derided the use of guaiacum as useless and expensive, but instead promoted mercury (he also believed in gnomes, spirits and fairies). He and his peers believed in the interrelationships between the perceived seven planets, the seven Earth metals, and the seven major human organs, for example the Sun/gold/heart and Mercury/mercury/lungs. This allowed healers to prescribe metal-based treatments to target different areas of the body. The Mercury treatment, however, had terrible side effects causing neuropathies, kidney failure, and severe mouth ulcers with the loss of teeth, and many patients died of mercurial poisoning rather than from the disease.

In 1566 a visitor to King Charles of France gave the king a bezoar stone. These are found in the stomachs and intestines of animals and humans and are made from things that cannot be digested in the body, such as hair, and fibres from fruit and vegetables. The visitor insisted that it would cure all poisons, but when King Charles asked Ambroise Paré, his surgeon, Paré said that it could not possibly cure all poisons because a hot poison needed a cold antidote and vice versa. Paré then suggested a test on

a live patient! A cook in the King's court had been caught stealing fine silver and was sentenced to death by hanging. As an alternative, the cook was granted the opportunity to receive a poison followed by a bezoar as a potential antidote under the supervision of Paré. It was agreed that if the cook survived the poison, his life would be spared. According to records he died in agony seven hours later; thus, Paré proved that the bezoar stone could not cure all poisons. It was another triumph for experiment and enquiry, though not necessarily for the cook.

There was a definite waste-not, want-not philosophy amongst Renaissance healers who put to good use any available plants, minerals, scraps and waste products from human and animal bodies and even religions in their remedies. Monique Rossignol, in her book *Medecine et Medicaments au XVIe Siècle à Lyon (Medicine and Medications in Sixteenth Century Lyon)*, described the use of remedies of human origin (derived from faeces, urine, saliva, and ear wax), those of an animal origin (made from the milk, droppings, urine, fat, and body parts), vegetable medicines (compounded from herbs and other plants) and mineral medicines, fashioned from elemental matter. Who would not want to use a mixture of mud and earwax for treating that irritating migraine? It was believed that pig urine fought fevers, and the roasted flesh of kittens relieved jaundice. Meanwhile, the droppings of dogs and crows were prized for treating colic and dysentery, respectively. And if you got depressed from some of these remedies, there was always saffron to add to your meat and drink to raise your spirits. But you were warned that eating too much could cause you to die of "excessive joy". Spring water was infused with bruised saffron and used to remove drunkenness, which was lucky since alcohol was also an integral part of some remedies, from improving digestion, to defending the body from corruption and strengthening the body's natural heat

"Who would not want to use a mixture of mud and earwax for treating migraine?"

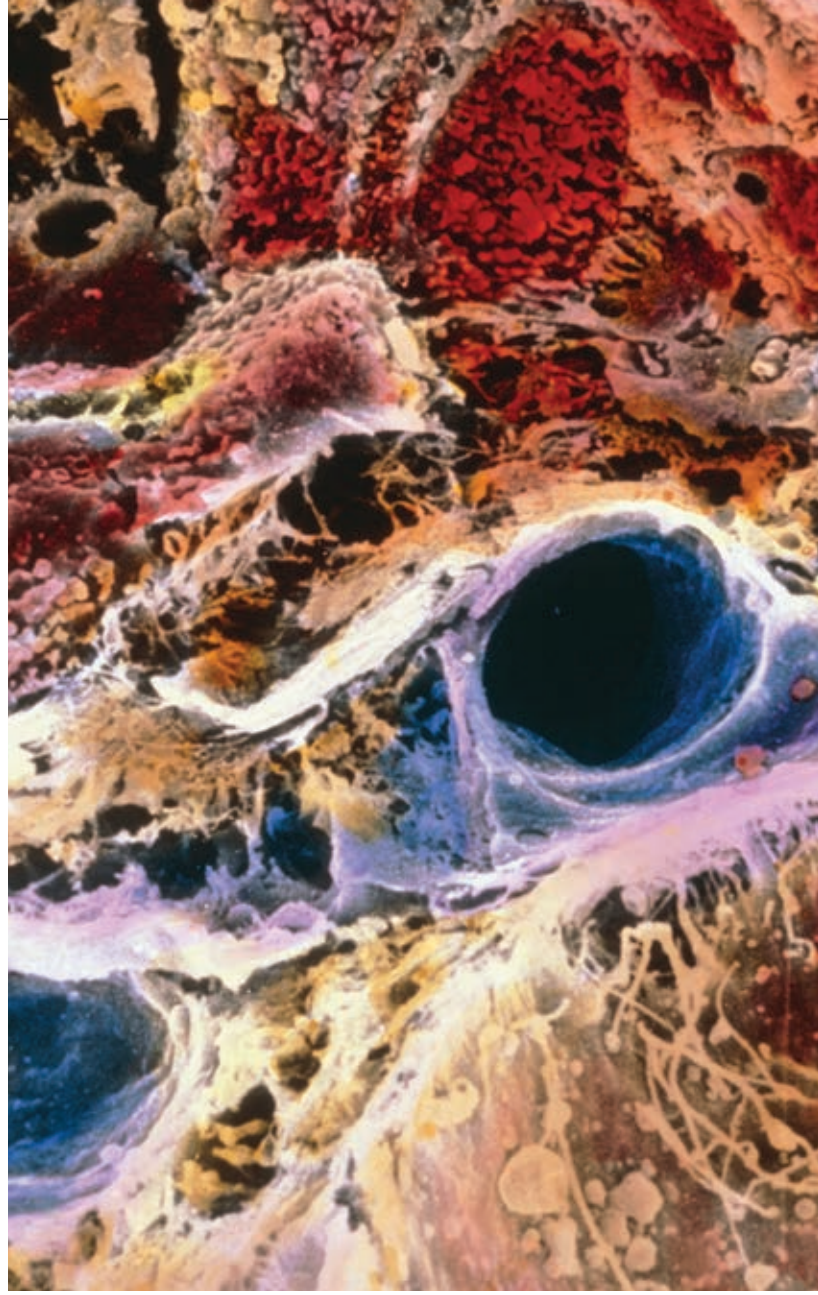
(alcohol flush?). Weakened patients could drink human blood, which was also available for leprosy sufferers as a salve for their scarred limbs and faces, but was loosely based on a study from the 11th Century where Valescus de Tharanta suggested "an ointment made from the blood of a young healthy person because the blood of a leper is corrupt".

End of the Renaissance

Everything must come to an end and by the end of the 15th century, the flower of the Italian Renaissance was beginning to wilt. Trade throughout northwest Europe had been disrupted by the Hundred Years' War (1337–1453) Italy was being torn apart by one war after another. The kings of England, France and Spain, along with the Pope and the Holy Roman Emperor, battled for control of the wealthy peninsula. There was also the expansion of the Ottoman Empire. King Edward III of England had reneged on his war debts, which had a ripple effect that caused the two largest Florentine banks (Bardi and Peruzzi) to collapse. This and the changing trade routes led to a period of economic decline and limited the amount of money that wealthy contributors could spend on the arts. There was a change in climate, which resulted in harsh winters and the decline of agriculture, which led to repeated famines and shortages. On the heels of a previous swell in the population, these shortages exacerbated the food shortages. The Black Death was still wiping out inhabitants in densely populated Northern Italian cities and it kept returning. As with any major health crisis in a city, disorder and pandemonium resulted.

The Catholic Church, which was racked with scandal and corruption, had begun a violent crackdown on dissenters. In 1545, the Council of Trent established the Roman Inquisition, which made humanism and any views that challenged the Catholic church punishable by death. Many Renaissance thinkers feared being too bold, which stifled creativity. By the early 17th Century, the Renaissance movement had died out, giving way to the Age of Enlightenment. BMS

Stephen Mortlock is the Pathology Manager at the Nuffield Health, Guildford Hospital. He would like to thank the Senior Management Team and all of the staff at the Guildford Hospital for their continued support.



BRITISH JOURNAL OF BIOMEDICAL SCIENCE

ISSUE 2 2020 – SYNOPSIS

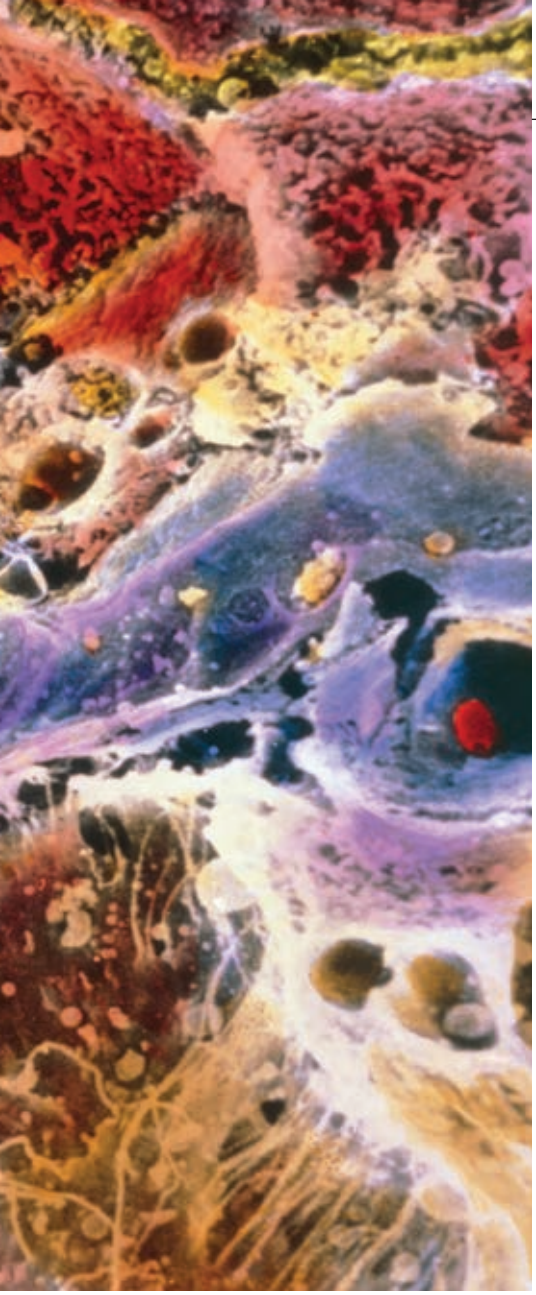
Deputy Editor **Guy Orchard** outlines the content in the latest issue, which includes a variety of subjects and a wide range of discipline-specific papers.

The study of cirrhosis and hepatocellular carcinoma (HCC) of the liver figure significantly in this issue. We start with Rowida *et al.*'s publication on the significance of a single nucleotide polymorphism (SNP) APa1 in the vitamin D receptor in HCC, arising from chronic hepatitis C virus (HCV) infection in liver cirrhosis. Employing a PCR-RFLP technique, the Apa1 CC genotype was found more frequently (75%) in HCC than in cirrhosis (35%) compared with standard controls. Providing evidence that Apa1 CC genotype is linked with HCC in HCV cirrhotic patients and could be used as a biomarker predictor for HCC occurrence in HCV cirrhosis.

Poor prognosis of HCC is often related to the late detection of the disease in its advanced stage. Here Attallah *et al.* hypothesise that collagen III and matrix metalloproteinase-1 (MMP-1) and their respective ratios are effective markers for early identification of HCC when used alongside serum alpha-fetoprotein (AFP), alkaline phosphatase and bilirubin. Here the authors assess 148 patients with HCC using imaging ultrasound and computed tomography and employ western blotting techniques on sera using ELISA. In HCC patients, collagen III and MMP-1 levels were higher than in fibrotic and cirrhotic control patient groups. Conversely HCC patients showed a lower concentration of MMP-1 than the control group. Liver function tests were abnormal; scores for AFP, alkaline phosphatase and bilirubin together with collagen III / MMP-1 ratio (CMR), termed the ABC test, were constructed and found to be statistically significant. As a result the authors conclude that the HCC-ABC test provided a promising index with a high degree of accuracy for HCC early detection and diagnosis.

Cancer stem cell markers

Next we take a look at the synergistic effects of CD44, a cancer stem cell marker, and the embryonic stem cell transcription factor Nanog on bladder cancer prognosis. The authors (Siddiqui *et al.*) take a look at the detection of CD44 in the basal layer of urothelial carcinoma and Nanog in bladder cancer employing immunohistochemistry on 112 bladder cancer cases. It was found that there was a significant correlation between the two markers in that bladder



patients with a high CD44 and Nanog expression had poor recurrence-free survival and poor overall survival. A combined index of CD44 and Nanog expression was felt to be a prognostic predictor of recurrence-free survival and overall survival in bladder cancer.

Gastric cancer

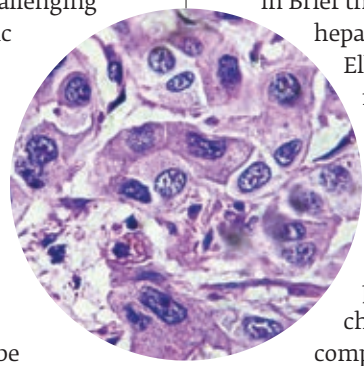
Following on from this we read the paper by Raad *et al.* on the association of rs2620381 polymorphism in miR-627 in gastric cancer. miRNAs are small endogenous non-coding RNAs with a length of 18-25 ribonucleotides that play important roles in cancer-related biological mechanisms, including cellular proliferation, apoptosis, angiogenesis, migration and invasion. A total of 280 healthy control patients were assessed in conjunction with 240 gastric cancer patients. Using genotyping by allele, specific PCR in conjunction with *in silico* analyses were carried out. Any C genotypes in rs2620381 were found to be linked to gastric cancer. There were no links between age, sex, tumour type, distant metastasis and tumour stages and miR-627 polymorphism in gastric cancer patients, thus providing evidence that the presence of the C single nucleotide polymorphism (SNP) in mIR-627 rs2620381 is linked with gastric cancer.

Cervical cancer

Kushwah *et al.* report on the study of cytokine gene variants and treatment outcomes of cicplatin-based concomitant chemoradiotherapy in cervical cancer. Cervical cancer remains the most common cancer among women world-wide after breast cancer. Standard treatment for cervical cancer is cisplatin-based concomitant chemoradiotherapy. By studying cytokine (IL-1, IL-6 and TNF gene) expression within the chronic inflammation in uterine cervix they found that SNPs in IL-1RN, IL-1b, IL-6 and TNFa were linked with cervical cancer. It was postulated that certain cytokine gene variants may help detect susceptibility to cervical cancer and further predict responses to chemoradiotherapy.

Chronic bacterial inflammation

A case study by Mohaghegh *et al.* on xanthogranulomatous pyelonephritis (XGP) masquerading as cystic renal cell carcinoma highlights a challenging case of XGP – a rare chronic bacterial inflammation of the renal parenchyma. Originally reported as a case of renal cell carcinoma, this case study highlights the diagnostic pitfalls of managing patients with XGP and explains why partial nephrectomy may be appropriate in the management of selective XGP patients.



Hepatitis C

Again we look at the value of SNP, this time as a Biomedical Science in Brief paper on rs12979860 and rs8099917 in IL-28B, and spontaneous clearance of hepatitis C genotype 4. Hepatitis C virus (HCV) is associated with liver disease worldwide with an estimated 170 million infected cases. A study by Mansoura University, Egypt compared 100 patients with HCV antibodies two or more times with positive HCV-RNA by real-time PCR two or more times over six months and elevated alanine aminotransferases (ALT), with 100 patients positive for HCV-IgG at two or more times and negative HCV-RNA by real time PCR within six months and with normal ALT. Evaluation of liver function tests and employing DNA extraction and amplification of rs8099917 and rs12979860, it was found that there was a marked differences in genotypes and alleles in both rs12979860 and rs8099917 in the two groups – those with TT genotype and T allele in rs12979860 were more likely to have chronic hepatitis C, while those with the TT genotype and T allele in rs8099917 were more likely to have spontaneously cleared the virus. It was concluded that an early stage of therapy in patients with an unfavourable IL28B genotype would be beneficial.

Hepatocellular carcinoma

Continuing in the Biomedical Science in Brief theme of studies on hepatocellular carcinoma, Elbaz *et al.* investigated the role of malondialdehyde (MDA) and C-reactive protein (CRP) as prognostic markers of hepatocellular carcinoma. A total of 180 patients with HCC and chronic HCV infection were compared with 180 age- and

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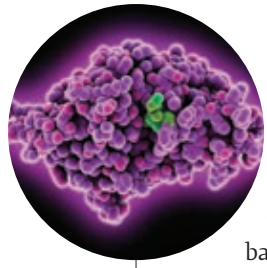
sex-matched cirrhotic chronic HCV patients free of HCC. In this group, serum levels of CRP and MDA were studied. MDA is a low molecular weight aldehyde produced by the attack of free radicals to polyunsaturated fatty acids during cellular membrane phospholipid degradation. A significant increase in serum CRP, MDA, bilirubin, AFP and AST levels were found in HCC patients. CRP and MDA were found to be the strongest differentiators of the two groups. The study revealed that serum levels of MDA were higher in patients with HCC versus the control cirrhotic group. In addition, MDA was higher in HCC patients with tumour sizes >5cm. The same pattern was found for levels of serum CRP, suggesting that CRP is also an indicator of poor prognosis among patients with HCC.



Carbapenemase-producing Enterobacterales

The second edition finishes with a third Biomedical Science in Brief paper, by Cafferkey *et al.*, on improving the processing time for the detection of carbapenemase-producing Enterobacterales (CPE) using an evolving algorithm. Recognising CPE is challenging in a routine diagnostic laboratory. Here, the authors present an interesting immunochromatographic-based algorithm assay to confirm CPE production with a modified carbapenem inactivation method test validating negative tests. This approach also demonstrated reduced processing times by demonstrating increasing numbers of isolates.

CPD

One of these articles may be the subject of a Journal-based learning exercise for those seeking to improve their continuing professional development profile. BMS

INTRODUCING: THE JOURNAL EDITOR AND THREE NEW DEPUTY EDITORS

Dr Andew Blann (Ed)

Andrew began life in the NHS as a Junior A MLSO in London in 1974, obtaining an ONC, two HNCs and FIBMS in immunology. As Senior MLSO he completed an OU degree and MSc in Rheumatology, and was awarded his PhD in 1995, joining the Institute's Haematology Advisory Panel, and the Editorial Board of our journal.

In 1997 he was appointed Principle Clinical Scientist/ Lecturer in Medicine at City Hospital, Birmingham, obtaining MRCPath in 1999. By 2003 he had become Senior Lecturer/Consultant Clinical Scientist, the following year FRCPath, and by 2008 was examiner in Haematology at the Royal College of Pathology and IBMS Deputy Chief Examiner in Haematology. Taking early retirement from the NHS in 2015, he focuses on teaching, writing, and editing the journal.

Dr Nigel Brown

Nigel started work as a Junior B MLSO in 1982, obtaining FIBMS in Clinical Chemistry in 1986 after taking his BSc at Newcastle University. In 1991 he became a Research Assistant at the Institute of Psychiatry (London), obtaining an MSc and then PhD. In 1999 Nigel moved back to the NHS as a Clinical Scientist in a specialist service measuring immunosuppressive drugs for routine clinical management and research.

In 2011 Nigel returned to the North East to run the Toxicology Laboratory at Wansbeck Hospital, and in 2014 was awarded FRCPath in Analytical Toxicology. This post includes being Duty Biochemist for the trust biochemistry service.

Nigel regularly liaises with services outside the laboratory including coroners, social services, public health and the local mental health trust.

Dr Guy Orchard

Guy runs the dermatopathology, Mohs' and trichogram services for Viapath Analytics at Guy's and St Thomas' NHS Trust. He lectures to biomedical science students at several universities, is the IBMS Chief Examiner for Cellular Pathology and sits on the IBMS/RCPath conjoint boards for reporting and histological dissection.

Guy completed his Fellowship in cellular pathology in 1990 (winning the RJ Lavington Prize), Master's in immunology at University of Surrey in 1995 and a PhD in 2010, receiving Chartered Scientist recognition in 2005. Guy has won two international awards from the National Society of Histotechnologists: in 2015 the Leica Leadership Award for Teaching and Education and in 2019 the Leica Leadership Award in Management and Training. Guy is also a member of three other scientific editorial boards.

Dr Anthony Rhodes

Tony is currently a professor in the School of Health Sciences at the International Medical University, Kuala Lumpur, Malaysia.

Tony's first post was as MLSO at The London School of Hygiene & Tropical Medicine where he obtained his FIBMS. He then worked at St Thomas' Hospital and then as Senior BMS at Hammersmith Hospital, during which time he obtained a master's in Medical Molecular Biology. His final post, before moving to academia, was as UK NEQAS Manager at UCL where he obtained his PhD.

In 2003, Tony moved to UWE, Bristol to teach Cellular Pathology and later appointed as Professor in 2010. In 2014, he moved to the University of Malaya as Professor in the Department of Pathology. Tony was awarded FRCPath in 2018.

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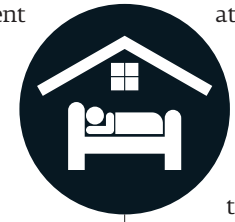
SCIENTIFIC LABORATORY SUPPLIES

AN AGEING WORKFORCE

Biomedical Science Professional Managers **Mairiead MacLennan** and **Jenny Smith** look at the impact staff demographics can have on the delivery of laboratory services.

The extended retirement age is having an impact on NHS staff and those working in laboratories are no exception. Shift patterns impact significantly on individuals who perform 12-hour shifts, which the unions advise against.



For biomedical scientists, there are a variety of shift patterns in place, dependent on the requirement for an out-of-hours service. Most blood sciences laboratories need to be staffed by at least three people carrying out all-night sample processing. Other laboratory services, such as microbiology, provide on site 24-hour services. Some larger microbiology departments are staffed by one or two biomedical scientists, but many are staffed with biomedical scientists and support workers for an extended day, then a biomedical scientist provides on-call service from home at night.

Severe pressure

The biomedical scientist who is on call from home may be woken from sleep to attend the laboratory to undertake critical tasks. Some departments experience such busy on-call services that the biomedical scientist is, in effect, working 12-hour shifts before managing to get home. Compensatory rest on the day following on call is variable across departments, with some departments relying on staff attending work the following day, if not called out after midnight.

If you are fit, healthy and resilient, this is manageable, but otherwise this sleep disturbance can impact on the general health of individuals. The knock-on effect can lead to absence through stress or other ill health.

Some shifts are under severe pressure due to the lack of experienced staff. The knock-on affect of compensatory rest is shortages of experienced staff on core day shifts. With the additional requirement to demonstrate substantial financial savings, the likelihood of securing increases to staffing cohorts is extremely low.

We are training excellent new recruits, however, that also takes time and it needs a full cohort of staff to release the trainers to meet the requirement. Some departments have as many as 20% of staff in primary specialist training. Experienced staff tend not to move because the nearest alternative would mean uprooting house and home. There are high numbers of experienced staff currently being lost, mostly to early retirement, and with this we are also losing their extensive knowledge and training expertise from departments.

The requirement

Laboratory services across the country are also facing the reality that the staff cohort currently providing the out-of-hours cover are expected to work until a retirement age of 66 or 67 years old and we will have to consider if this is sustainable and how we will manage out-of-hours services in the future.

Some staff simply cannot continue to provide the on-call shift for health or other reasons, such as caring commitments (children or elderly parents), and as the demographic ages, more and more staff are likely to find this increasingly difficult.

Management teams have to review the

shift patterns and closely examine the terms and conditions alongside expectations of staff to decide whether reasonable adjustments can be made. The NHS aims to provide the most flexible working arrangements possible. However, the question arises of equitable arrangements for all and who will be the gatekeeper?

Should an agreed age cap be introduced for on-call work, with those who wish to continue able to do so? It would take the guilt, anxiety and pressure off those who are simply unable to sustain on-call work.

The needs of the service also require to be considered. Should a biomedical scientist be called out in the middle of the night to look up a LIMS results for a urine antimicrobial sensitivity test? The information is readily available on the system and it isn't an urgent requirement. The information can be communicated by day staff at 8am. However, the person has already been awoken and is unlikely to get back to sleep immediately. Strict adherence to well-discussed and agreed policies between the users in the hospital and the laboratory is key. The Consultant Microbiologists usually also have to be at work the next morning after an on call overnight. Some national guidelines would be advantageous. The service provided at hospitals differs greatly, but it would provide confidence across the services to have agreed overnight laboratory service provision.

Supporting the service

Laboratory services are well aware of the lack of knowledge and awareness from our nursing and medical colleagues about what happens in laboratories. I am sure the same goes the other way around. As professionals, we do need to learn more about each other's roles and how what we do impacts on them. We like to invite our colleagues to see for themselves and they are mostly stunned by how little they know about how the laboratories operate. However, if we are short of staff due to shift pressures, we may not be able to spare someone to show them around. A feature that impacts on many departments, given that the majority of biomedical scientists are female, is maternity leave. The legislation is excellent and enables new mums to spend up to a year with their babies before using retained annual leave to phase their return. However, such absences do not receive backfill funding.

Organisations must support the laboratory service to ensure they can maintain an appropriate service. If an increased staff cohort is not supported, and spend on new technology and rapid diagnostics is limited, then a reduction in service is inevitable.

Debate does need to centre on what is the right test, right place, right TIME, but we also have to consider what is going to happen with the result of the test. Will there be clinical staff available to receive the result and are they going to act upon it? Let's use our limited resources to deliver the highest impact service exactly where it is required and ensure the users know what that is and is not. BMS

Dr Mairiead MacLennan is a Biomedical Scientist Professional Manager in Quality and Training. **Jenny Smith** is a Biomedical Scientist Professional Manager. Both are based at Victoria Hospital in Fife.

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MICROBIOLOGY IN RURAL INDIA

Former Chief Biomedical Scientist **Ivor J Mitchelmore** outlines a trip to India, where he and colleagues worked to set up a microbiology culture service.

Earlier this year, along with two ex-microbiology colleagues, Hilary Rogers and Ruth Parry, I visited a small mission hospital in the village of Sarenga, West Bengal. It is called Khristiya Seva Niketan (KSN) hospital and serves a large rural population, mainly of tribal people.

Maternity and children make up the majority of inpatients, plus there are busy outpatient clinics. While we were at KSN, they held an eye camp, at which over 40 cataract operations were performed. Building work has started for a blood bank, which will enable KSN to perform more complex surgery. The hospital already has a small pathology laboratory offering a basic range of haematology and biochemistry tests, but no microbiology culture service. This means that patients with suspected infections are treated blind, with nothing to say whether the treatment is appropriate other than observing their condition.

Better prepared

On a visit to the hospital in 2018, the Medical Superintendent and other doctors at the hospital said that they would value the setting up of a microbiology service. Having had a disappointing experience last year, when I spent the first three months at KSN trying to help them set up microbiology testing, I was determined this time.

The three of us all had our maximum luggage allowance of 40kg each, and over half of this was due to donations of equipment and consumables from companies and local laboratories.

I had earlier shipped out a benchtop autoclave, which proved invaluable. Yes, you can buy an autoclave in India, but will it work? After trying three last year, all of which failed, I decided to take one that I knew would do the job.

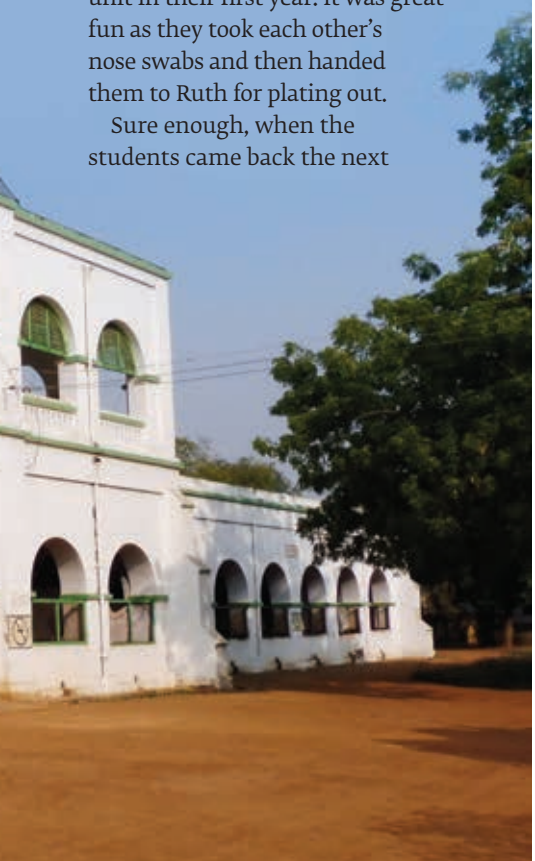
Hilary had recently retired after 37 years service at the Luton and Dunstable

Hospital, and is an expert in media production (along with bacteriology, mycology and parasitology). Within a few days, we had a fridge full of culture media. This was almost entirely produced by the local staff under Hilary's supervision. I was thankful that we did not have to resort to bleeding the staff to make the blood agar plates (as happens at another hospital I have visited in India), but instead we managed to obtain an expired pack of blood from a blood bank.

Obtaining samples

We had taken a few blood agar and Mueller-Hinton agar plates with us, and immediately set up nose swabs from the lab staff, in the hope of obtaining a *Staphylococcus aureus* control. We drew a blank there, but then had the idea of swabbing all the 25 first-year nursing students from the nurse training school attached to KSN. This turned into a lab-based training session for the students, who have a large microbiology unit in their first year. It was great fun as they took each other's nose swabs and then handed them to Ruth for plating out.

Sure enough, when the students came back the next day, several of their nose swabs had grown *S. aureus*, as confirmed by the staph latex kit and rabbit plasma we had brought with us. One girl was horrified to discover she had *S. aureus* in her nose, and we explained to her that it was normal for some people.



For training purposes we inoculated a rectal swab onto a range of plates, which served to demonstrate *Proteus* swarming, and provided a *Pseudomonas* and a lactose-fermenting coliform as control organisms. We also isolated our first anaerobic bacteria, using an anaerobic jar.

To create a CO_2-enriched atmosphere, we used a candle in a sealed biscuit tin. From a catheter specimen of urine we were able to isolate Group B beta-haemolytic streptococci from the mixed growth. We now had positive and negative control organisms for slide and tube coagulase, staph latex, oxidase and catalase tests plus the Group B streptococci to control the strep latex procedure – very important to enable local staff to practise their newly learnt skills. With the control organisms we had gathered, Ruth organised training the staff in making and reading Gram-stained films. With limited resources, this will be a key step in identifying their isolates.

CONTRIBUTIONS

Ivor J Mitchelmore is a former Chief Biomedical Scientist in the department of medical microbiology at Luton and Dunstable Hospital. He would like to thank the following companies and laboratories for their contributions to the project: BioConnections, Don Whitley Scientific, Mast Group, Medical Wire, Pro-Lab Diagnostics, Department of Medical Microbiology at Luton and Dunstable Hospital and the Department of Microbiology at Watford General Hospital.

The most satisfying result was when the obstetrics and gynaecology doctor sent a urine sample from a patient visiting the weekly antenatal clinic. It had a high white cell count and the following day we had grown what looked like a fully sensitive *Escherichia coli*. The same result would have taken five days if we had sent it to an outside laboratory. This was processed by local staff and the patient was started on nitrofurantoin, but later admitted and changed to IV gentamicin. She made a complete recovery.

We have since grown urine isolates that have been resistant to five out of six antibiotics tested, so it shows the importance of checking the susceptibility patterns of these organisms.

Tremendous progress

As well as the practical work I gave regular half-hour presentations to staff, explaining the theory behind what they had been learning at the bench. I don't speak much Bengali, so there was a language barrier, but the staff all speak some English and the younger ones are very good at explaining things to the others, where necessary.

Ruth and Hilary returned to the UK after two weeks, but I could not have achieved the tremendous progress we have made without them, or without the generous contributions from the trade and local UK laboratories (see box). I had to keep reminding myself that in seven weeks we were expecting the local staff to pick up skills that took me a year to begin to get to grips with. The lab staff at KSN have done incredibly well, but still need a lot of support.

Time will tell how effectively this can be delivered via WhatsApp. I am already thinking about a November visit to give some booster sessions, and take them to the next level. At least now I have the confidence to know that change is possible. BMS

MY IBMS NEWS

STEM FOR BRITAIN

2020 award winners revealed

Early career researchers took centre stage at this year's STEM for Britain awards.

The annual awards were set up to recognise and showcase outstanding research by scientists at the start of their careers.

Since 2012 the IBMS has been a proud sponsor of the gold and silver awards for the biological and biomedical sciences categories.

The winners this year were:

GOLD – **Sarah Houston**, Institute of Ophthamology, University College London, for her poster "Using the eye as a window to the brain in multiple sclerosis".

SILVER – **Karoliina Tuomela**, Lydia Becker Institute of Immunology, University of Manchester, for her poster "Radiotherapy can make cancer cells resistant to immune cell attack".

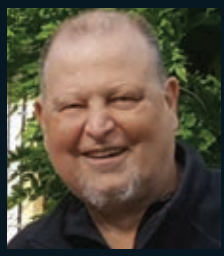
BRONZE – **Ted Roberts**, School of Biochemistry, Biomedical Sciences, University of Bristol, for his poster "Culturing neutrophils from stem cells to explore neutrophil cell biology and disease".

IBMS President Allan Wilson addressed the audience. He said: "I think that opportunities for biomedical scientists are set to expand considerably. If our health services are to maintain the expected high standards of care, new and emerging roles will be crucial, and we need innovative scientists like yourselves.

"This year we were very impressed with the quality of research on display from the three winners of the biological and biomedical sciences category."

OBITUARY

STEVE CRANE

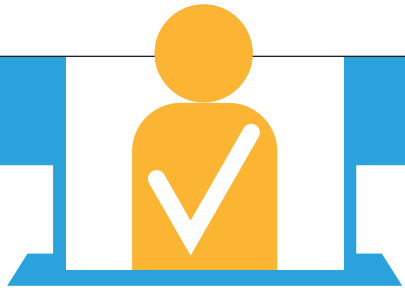


It is with a sad heart that I have to write this. Steve passed away on 30 December 2019. He had struggled against illness for some time until his enormous energy ran out and it was time to say goodbye to this world.

I first met Steve on the first day of the first Diploma in Medical Laboratory Management course. He was teamed up, perhaps not so fortunately, with me, Christine Cranmer and Dianne Smith. From that point on we had a lasting friendship. He was a man of many sides: Hairy Biker with matching beard, liked beer, wine, port and had a zest for life that got him to the top of many things, including mountains.

Above all else, Steve was a family man devoted to his wife Ann and their three children, Megan, Bryony and Bethany. He started work at the West Middlesex Hospital, beginning his career there in 1973 and then on to Watford General Hospital, the EE2 Welwyn Garden City and he became manager of the histology department at the Royal National Orthopaedic Hospital where, towards the end of his career, he did many incredible feats of skill and dexterity to get sections from impossible specimens. He was a 'Mister Fix-it' for many people with his calm manner and boundless enthusiasm for his work. He was the same in life: kind, thoughtful and generous to a fault. He pushed the boundaries in many areas of his life, most notably in cooking his cuisine, sometimes being a gastronomic adventurer. He was our brother in and outside of pathology and did so much more, being founder member of the London Management Group. Fix-it in work, fix-it at home and when faced with the challenge of not being able to buy what he liked he just made it. He had, at home, the best 'shed' ever, with tools to do any job. Could you imagine a five star camper van made by a genius? He loved life, walking, mountaineering, motorcycling, food and cooking with his favoured barbecue method and travelling in his camper van with his wife and children. A friend, a colleague, a man of intellect and broad thought that filled your time and drove your imagination. There was no other like him. We shall miss him more than words can convey.

Jerry Cox
Friend and former colleague



VOTE FOR YOUR COUNCIL

The IBMS Council is the Institute's governing body and comprises six National and 12 Regional members. It is elected by members to make key decisions, develop policy and strategy, and ensure the organisation achieves its aims and objectives on behalf of IBMS members. Council members will play a central role in shaping the Institute's future and ensuring that the professional body is run effectively and that it meets members' needs.

The following nominations were received by the due date to fill the vacancies on Council in 2020.

REGIONAL MEMBERS - TWO VACANCIES

WALES

- Dr Victoria Bradley

No ballot will be required for Wales.

SOUTH EAST

- Dr Jane Needham
- Clare Bailey

Elections for the South East vacancy will be required.

NATIONAL MEMBERS - TWO VACANCIES

- Helen Archer
- Zanya Jeffrey
- Charlie Houston
- Joyce Overfield
- Sheri Scott

Elections for the National vacancies will be required.

ELECTIONS – HOW TO VOTE

Corporate members who have previously registered an email address with the Institute will receive an email containing their secure link to the voting site on 22nd April 2020.

Corporate Members who have not registered their email address with the Institute may register to receive their voting details by email using one of the following methods. Your full name and IBMS membership number will be required.

BY EMAIL support@mi-voice.com

By phone: 023 807 6 3987 (this service will be staffed from Monday to Friday, 9.00am – 5.30pm excluding Public Holidays and a voicemail service is available at other times)

BY INTERNET www.mi-nomination.com/IBMSBallotRequest

Voting will close at 5.00pm on Thursday 21 May 2020

ALL ELIGIBLE MEMBERS ARE ENCOURAGED TO VOTE

PANDEMIC

COVID-19 RESOURCES

The IBMS has provided a series of resources for professionals about COVID-19.

There is a new resource section on the website dedicated to informing professionals with the latest information and guidance.

These resources include guidance, official statements and comments from professional bodies and organisations, including the NHS and Public Health England.

This resource section will be updated with new documents as more information becomes available.

→To access the resources, visit ibms.org/resources/covid-19-resources

QUALITY AND ACCREDITATION

NEW QUALITY AND UKAS PODCAST OUT NOW

A new episode of the IBMS podcast is now available to stream, online.

The podcast covers accreditation and quality management and features Ben Courtney from UKAS and Debra Padgett, a Pathology Quality Manager from North Cumbria University Hospitals NHS Trust.

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

It is the sixth episode of the podcast and all previous episodes can still be accessed on the website.

These range from Dr Sarah Pitt talking about snail slime and virology, to Professor Barbara Bain on morphology.

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

PROFESSIONAL PROMOTION

BIOMEDICAL SCIENCE DAY

Biomedical Science Day was due to take place on 11 June, but has been postponed due to COVID-19.

A new date will be announced in due course.

→ For updates and further information, keep an eye on the IBMS website and social media pages.

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 1 JULY 2020

Association of SNPs in *PLA2R1* with idiopathic and secondary membranous nephropathy in two Chinese cohorts Tian CX, Li L, Qiu P, Qiu YR. *Br J Biomed Sci* 2020; **77** (1): 24–8. Assessment No A101020

01	About 70% of membranous nephropathy (MN) patients have idiopathic MN (IMN) one of the most common types of primary glomerulonephritis.	11	The authors previously reported that 71.7% of patients with IMN and 9.3% of patients with SMN were PLA2R-Ab+
02	Diseases such as systemic lupus erythematosus (SLE) hepatitis B and hepatitis C infections, and malignancies, are major causes of IMN.	12	The rs35771982 single nucleotide polymorphism (SNP) within *PLA2R1* had the strongest association with IMN in cohorts from Korea, South Asia, Taiwan, China and Japan.
03	About 35% of refractory MN patients develop end-stage renal disease within five years.	13	Saeed *et al.* reported no association between rs35771982 and IMN in a cohort of PLA2R-Ab+ African Americans.
04	Idiopathic MN is now considered to be an autoimmune disease that targets the kidneys, in which there are circulating autoantibodies.	14	The rs3749117 SNP within *PLA2R1* is less common in cohorts of white Europeans with SMN, and in Caucasians, African Americans and Japanese who are PLA2R-Ab+
05	Serum anti-PLA2R antibodies were measured using a commercial direct immunofluorescence staining kit.	15	The rs3828323 SNP within *PLA2R1* is in a coding region of exon 5.
06	Genomic DNA was isolated from peripheral blood leucocytes using a DNA isolation kit obtained from Euroimmun.	16	Chinese individuals with the rs4664308-A allele had an increased risk of SMN, but those with the rs4664308-G allele had an increased risk of IMN.
07	Amplification was performed on an ABI Vii7 Dx real-time polymerase chain reaction (PCR) system from Applied Biosystems.	17	The rs3749119 SNP within *PLA2R1* is in the 5'untranslated region of exon 1.
08	Genotype and allele distributions of rs35771982, rs3749117 and rs4664308 differed significantly between IMN patients and controls.	18	The circulating level of anti-PLA2R autoantibody is a highly specific diagnostic biomarker for IMN.
09	All groups were age- and sex-matched, and differences in serum creatinine were as expected, although there were no differences in serum albumin.	19	In this study, group B comprised 166 IMN patients and 144 healthy controls.
10	Genotype and allele distributions of rs3749119 and rs3828323 showed significant differences between IMN patients and controls.	20	The A allele in rs35771982 and the C allele in rs4664308 were associated with PLA2RAb+ in IMN patients from Hubei Province in China.

REFLECTIVE LEARNING

01	Idiopathic membranous nephropathy is now considered to be an autoimmune disease. Choose another common autoimmune disease and discuss the role of molecular testing in the laboratory assessment of the condition.	02	Explain the meaning of the term idiopathic in relation to primary glomerulonephritis, and how this compares to secondary MN disease.

DEADLINE WEDNESDAY 1 JULY 2020

British Journal of Biomedical Science in 2019. What have we learned?
Blann A. *Br J Biomed Sci 2020;* **77** (1): 1–6. (Assessment No: MDJBL11)

01	75% of the 39 papers published in *BJBS* employed either RNA and/or DNA techniques.	**11**	Warford and colleagues showed that in the determination of clonality in lymphoma, diagnosis can be aided and improved by employing branched DNA *in situ* hybridisation for light chain mRNA.
02	The liver was the tissue /organ type studied most over the year's publications.	**12**	The new wave of molecular genetics is based on two main types of non-coding RNAs: micro-RNAs (mRNAs; individual molecules generally identified by Mir followed by a number) of around 22 nucleotides, and long non-coding RNAs (Including RNAs) of at least 200 nucleotides.
03	In El-Bendary and colleagues' paper, *CCL2* and *CCR2* genes were linked with susceptibility to herpes virus C single nucleotide polymorphisms.	**13**	When measuring the micro-RNA (miR-935) in non-small cell lung cancer and comparing to nearby normal lung tissue, the significance for patients with the lowest levels is that they are less likely to have lymph node metastasis.
04	Platelet-derived growth factors and albumin may be important in combination in determining the extent of hepatic fibrosis.	**14**	In the study by Abdullah and colleagues looking at age-related cataracts, miR-15a was found to be increased in expression within the lens epithelia.
05	In terms of non-alcoholic fatty liver disease, only age was linked with the development of urolithiasis.	**15**	In a study published in the journal by Aminian and colleagues on lncRNAs expression in gastric cancer, they discovered a reduced frequency of a deletion allele in the target sequence in lncRNA GA55 in patients' DNA.
06	In terms of diabetes, only hypertension is regarded as a major clinical feature.	**16**	In a study published by Dou and colleagues on *Klebsiella pneumoniae*, they discovered an advance in detection when using multiplex PCR towards an organism-specific gene, *rcsA*, and 23S rRNA.
07	Septicaemia is linked to alterations in white blood cell count, neutrophils, platelets, cytokines, creatinine and acid base.	**17**	In the study of the pathogenicity of *Helicobacter pylori* in gastric disease, two types of genes, *gag* and *fro*, have been implicated.
08	In terms of cellular and tissue damage responses in septicaemia, Kumar and colleagues provided evidence to support the role of neutrophil-derived reactive nitrous oxidative stress.	**18**	In the study by Pitt and colleagues on the antibiotic potential of snail mucus, they discovered a number of proteins that inhibited the growth of *Pseudomonas aeruginosa*. The most promising was a 35.4 kDa molecule called Aspernin.
09	The presence of melanin pigment in malignant melanomas does not mask antigen-antibody interactions.	**19**	In the work by Lucejko and colleagues studying hepatitis viruses and liver disease, they compared quantitative measurement of HCVag with that of HCV RNA in HCV-infected patients, and discovered that the immunoassay could be a viable option to nucleic acid assessment.
10	In Orchard's paper, the use of immunohistochemistry to demonstrate V600E *BRAF* mutations in malignant melanoma had a sensitivity of 100% and specificity of 80%.	**20**	In the paper published by Shabani and colleagues on andrology investigations, it was reported there was a possible role in the study of SNP (single nucleotide polymorphism) molecular alterations/mutations in the study of glial cell-derived neurotrophic factor (GDNF), which has an important role in spermatogenesis in male infertility.

REFLECTIVE LEARNING

01	What is the value of studying single nucleotide polymorphisms in the evaluation of disease pathogenesis?	**02**	What are the problems faced when performing immunohistochemistry on heavily pigmented melanocytic lesions? Discuss how these can be overcome.

EVENTS AND TRAINING COURSES

IBMS Institute of Biomedical Science Continuing Professional Development

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

DATE	TITLE	VENUE CONTACT
April		
3 Apr	**Clinical Biochemistry Short Course 3**	London I c.ferrier@westminster.ac.uk
7-9 Apr	**BSAC Residential Workshops for EUCAST Susceptibility Testing**	Cardiff I ecarruthers@bsac.org.uk
15 Apr	**UK NEQAS Cellular Pathology Technique Introduction to Immunocytochemistry Workshop**	Northumbria I cpt@ukneqas.org.uk
16 Apr	**UK NEQAS Cellular Pathology Technique Advanced ICC Applications in Laboratory Practice A Workshop**	Northumbria I cpt@ukneqas.org.uk
18 Apr	**Biomed Online Learning courses**	Online I c.e.ronan@gre.ac.uk
20 Apr	**UK NEQAS immunology, immunochemistry and allergy: neuroimmunology discussion group meeting**	Birmingham I ukneqas@immqas.org.uk
24 Apr	**Association of Anatomical Pathology Technologists and Human Tissue Authority Consent Training Day**	London I christianburt@ibms.org
25-27 Apr	**BSAC Residential Workshops for EUCAST Susceptibility Testing**	Cardiff I ecarruthers@bsac.org.uk
27-29 Apr	**British Society for Haematology 60th Annual Scientific Meeting**	Petersfield I BSH2020@mci-group.com
28-30 Apr	**Human Genome Engineering using CRISPR/Cas9**	London I k.surendranath1@westminster.ac.uk
May		
6 May	**UK NEQAS Cellular Pathology Technique Non Gyn Cytology Beginners/Refresher Workshop**	Gateshead I cpt@ukneqas.org.uk
7 May	**UK NEQAS Cellular Pathology Technique Non Gyn Cytology Intermediate Workshop**	Gateshead I cpt@ukneqas.org.uk
13 May	**UK Standards for Microbiology Investigations - Chairs Strategy Working Group Meeting May 2020**	London I Public Health England
14 May	**The Genomic & Microbiology Revolution: in Technology we Trust (or do we?)**	Hendon I swallis@mastgrp.com
18 May	**Masterclass Cryoglobulin Analysis and Interpretation**	Birmingham I ukneqas@immqas.org.uk
20 May	**UK NEQAS Cellular Pathology Technique TEM workshop**	Leicester I cpt@ukneqas.org.uk
June		
3 Jun	**IBMS Registration Portfolio Workshop**	London I c.ferrier@westminster.ac.uk
3-4 Jun	**Clinical and Laboratory Haemostasis 2020; UK NEQAS for Blood Coagulation Annual Scientific Meeting**	Sheffield I tim.woods@nhs.net
10-12 Jun	**The Laboratory Diagnosis of Malaria**	London I claire.rogers@lshtm.ac.uk
15-19 Jun	**Cryo Electron Microscopy Course 2020**	Rothamsted Research I katejermey@rms.org.uk
15-19 Jun	**The Laboratory Diagnosis of Parasites**	London I claire.rogers@lshtm.ac.uk
17 Jun	**UK NEQAS Cellular Pathology Technique Introduction to Specialist Demonstration Techniques**	Northumbria I cpt@ukneqas.org.uk
18 Jun	**UK NEQAS Cellular Pathology Technique Specialist Demonstration Techniques A**	Northumbria I cpt@ukneqas.org.uk
18-19 Jun	**Practical and Clinical Microbiology of Anaerobes**	Cardiff I deborah_robinson@dwscientific.co.uk
19 Jun	**UK NEQAS Immunology, Immunochemistry and Allergy Annual Participants meeting 2020: Getting It Right Every Time**	Sheffield I ukneqas@immqas.org.uk

HERE TO HELP

CPD OPPORTUNITIES ARE EVERYWHERE

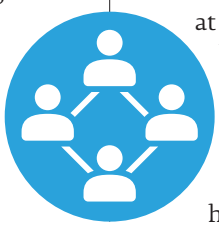
What can be classed as CPD? **Jocelyn Pryce**, Deputy Head of Education at the IBMS, looks at opportunities, barriers and a day of discussion.

It's always nice when we are able to engage with our members and facilitate the sharing of good practice. We were able to do this recently when we hosted a CPD Officer Event here at Coldbath Square.

The aims of the day were for our CPD Officers to understand what their roles and responsibilities may entail and how we can support them to support their colleagues in the laboratory, by describing what is meant by continued professional development, why it's important, what activities are acceptable to be used as CPD and what reflection is.

It was an interactive day and, as there's no such thing as a free lunch, we kept the presentations short and got everyone networking and sharing ideas. We looked at what CPD is and can be, finding out it can be almost anything. It doesn't have to be an event or conference, a lunchtime meeting or evening session – it is embedded in everything we do. You might use an incident, an audit, or even a conversation held in the tearoom if it has been a learning experience. My co-host Mike Carter explained that tearoom chat can be a great place to share knowledge and a learning experience, maybe not the latest gossip or events in Coronation Street but, for example, it could be sharing knowledge about COVID-19.

We also spent time considering some of the perceived barriers to undertaking CPD, including lack of time, geographical location, funding and support from management, and discussed ways that our CPD Officers may offer support to overcome them.



Our workshops were scenario-based and involved groups of CPD Officers sharing ideas for CPD within a scenario where they were the CPD Officer for a small laboratory, with a mixture of staff grades across two geographically remote sites. The outcomes were really impressive and showed that there are some great, innovative opportunities for CPD going on across the country.

Reflection is an area that can raise fear and dread and we spent time looking at why reflection is important, how valuable it can be and how to approach it in a painless way.

By the end of the day everyone had produced a piece of reflective writing and we had considered ways of using prompts to encourage those who find reflection difficult to capture their thoughts and feelings.

The networking nature of the workshops allowed sharing of ideas and attendees have access to the outputs to refer back to. Feedback on the day has been very positive, with a satisfaction rate of over 90%, and some of the comments we have received suggest that delegates took lots of ideas away with them and felt that they were well prepared to support their colleagues back in the laboratory.

As this day was so well received, we have decided to run some more during 2020, so if you are a CPD Officer or would like to become one, please keep an eye on our website or contact cpd@ibms.org for further details. IBMS

IMAGES: ISTOCK

MY LAB

THE FIRST UK LAB TO IDENTIFY COVID-19

Biomedical scientist **Martine Jensen** gives a guided tour of her lab at of the Hull University Teaching Hospitals NHS Trust.

The microbiology laboratory at Hull Royal Infirmary is part of the Hull University Teaching Hospitals NHS Trust and provides services to a wide geographical area. There is also a satellite laboratory at Castle Hill Hospital that provides virology services, including chlamydia and other STI NAAT work, HIV testing, viral loads and a whole host of other tests. The team processes approximately 360,000 samples a year. The service is provided by a diverse team of competent and motivated staff, including pathology support workers, associate practitioners, biomedical scientists, clinical scientists and consultants.

COVID-19 testing will soon be added to our testing repertoire – the first two coronavirus cases were submitted from our laboratory and the patients were initially managed at our infectious diseases unit. We are a unique service, with microbiology and virology working jointly with infectious disease physicians as one department of infection.

We host monthly discussion groups where lab staff and infectious disease doctors work together to present unusual or relevant case studies to all interested staff as part of the training and continuous development programme. Providing people with development opportunities ensures we have knowledgeable staff providing a high-quality and efficient service to the users.

Though this is a very busy laboratory conforming to ISO 15189, it is an IBMS- and NSHCS-accredited training facility and we make training our core business. Staff are encouraged to undertake and complete courses, such as specialist and higher specialist portfolios and certificates of expert practice. Individuals are carrying out Masters qualifications via distance learning and several staff are on degree apprentice schemes to become qualified biomedical scientists. Support workers are completing the IBMS Certificate of Achievement, while two biomedical scientists have achieved awards for obtaining the highest mark that year for their chosen subject in their respective Higher Specialist Diplomas.

With staff central to our success, the latest technologies are employed. Last year, PCR testing was improved by the addition of the Biofire FilmArray system. Using syndromic testing has highlighted to the trust the positive impact of rapid microbiology results in patient management and antimicrobial stewardship. We started to use the upper respiratory panel, covering 20 bacterial and viral pathogens, and this proved a success so we have moved to offering the lower respiratory (pneumonia) panel, which can provide quantified bacteria reports with resistance mechanisms alongside viral and atypical bacterial targets in just over an hour. We now use this technology to rapidly diagnose meningitis and encephalitis, and we are hoping to introduce the gastrointestinal panel in the near future.

It is amazing to see how rapidly technology is changing traditional microbiology and what a difference we can quickly make to our patients.

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I KNOW WE ARE SAVING LIVES

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