THE BIG QUESTION

POST-PANDEMIC LIFE

How public attitudes to health may change after the pandemic: *p.14*

BIOSTATISTICS

AN EDUCATED GUESS

Can we believe all the statistics we read about COVID-19? *p.24*

HISTORY

THE GREAT PESTILENCE

The first great pandemic to devastate these shores: *p.26*

THE BIOMEDICAL SCIENTIST

THEBIOMEDICALSCIENTIST.NET

MAY 2020

COVID-19

The search for a vaccine

IBMS Institute of Biomedical Science

EntericBio

CPE

Carbapenemase Producing Enterobacteriaceae screening assay for both rectal and isolate testing.

EntericBio CPE Targets

- OXA-48
- KPC
- NDM
- VIM
- IMP
- GES

EntericBio molecular system is rapid, reliable and easy to use, providing results within 3 hours. Users benefit by having lyophilised ready to use reagents, no requirement for DNA extraction and an automated setup now coupled with the introduction of automated results analysis. Serosep prides itself by providing class leading service through its dedicated technical support team.

According to CEO Mr. Dermot Scanlon, *"EntericBio has become a new gold standard test for gastrointestinal testing replacing culture method with eight out of every ten samples tested in Ireland, Northern Ireland and Wales now using this PCR test. The test is also widely used in the UK making EntericBio an overall market leader."*

SEROSEP

Contact us now at: serosep.com

CE IVD

CONTENTS

IBMS.ORG

MAY 2020

EDITORIAL

NEWS

OPINION

SCIENCE

COVER FEATURE

ADVICE

MY IBMS

MY LAB

EDITOR
Rob Dabrowski
SENIOR DESIGNER
Gary Hill
PICTURE EDITOR
Akin Falope
PUBLISHING DIRECTOR
Aaron Nicholls
PRODUCTION
Rachel Young
DISPLAY ADVERTISING
+44 (0)20 7880 7556
biomedical@redactive.co.uk

redactive

PUBLISHED BY
Redactive Publishing Ltd
Level 5, 78 Chamber Street, London E1 8BL
+44 (0)20 7880 6200 redactive.co.uk

Recycle your magazine's plastic wrap – check your local LDPE facilities to find out how.

4 LDPE

RECRUITMENT ADVERTISING
+44 (0)20 7880 7665
biomedicaljobs@redactive.co.uk

ISSN 1352-7673

PRINTED BY
Warners Midlands plc
Bourne, Lincolnshire PE10 9PH

SUBSCRIPTIONS
Subscriptions are available by calling 01580 883844

A.MENARINI diagnostics

MAGNUS

Same Day Processing

Lean. Economical. Flexible. Safe

- Fastest system on the market
- Ultra rapid and lean processing for same day diagnosis
- No downtime for daily maintenance
- Real-time reagent quality monitoring ensures best specimen integrity and reduces cost
- Minimises reagent use
- Enhanced specimen quality with optimised xylene and xylene-free protocols, for ALL specimen types and sizes
- Future proof with optional onboard embedding
- Xylene-free and reduced reagents improve environmental impact

www.totaltissuediagnostics.com

Telephone: 0118 944 4100
Email: enquiries@menarinidiag.co.uk

TOTAL TISSUE™ DIAGNOSTICS
From surgical specimen to diagnosis

RESPECT FOR THE PROFESSION

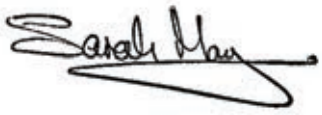
Deputy Chief Executive of the IBMS **Sarah May** feels both joy and despair at recent reactions to COVID-19.

We're living in extraordinary times, with every news channel and conversation dominated by the coronavirus pandemic. I've ground my teeth in frustration every time I see or hear that the testing is being performed by doctors and that all the spare laboratory space should be used to increase testing rates, but this week something has happened and my heart has soared.

During the lockdown the Institute's Council, staff and scientific advisors have been working flat out to respond to news items, correct misinformation and to provide good clear scientific explanation about COVID-19 diagnosis and the scientists who provide those diagnostic services. At last we have been recognised as the voice of a vital profession and our opinion and advice has been sought – our President, Allan Wilson, has been interviewed on both television and radio, giving clear professional advice and opinion (see p.43 for more information). It is a great pity that it has taken such an event as a pandemic to bring us to the fore, but it is our good fortune that we have Allan at the helm, as he has garnered much attention and respect both personally and for our profession .

A very different outcome of the coronavirus lockdown has been the realisation that homeworking, when enforced rather than an option, is not the luxury it might have once seemed. Our office in central London is closed and all staff are now working remotely. I appreciate that this is not an option open to many of our members, who are travelling in to work in hospital laboratories each day, but I miss my colleagues and realise that all the technology in the world is no substitute for a good face-to-face conversation. I am writing this as the Easter weekend begins and know that for everyone who isn't covering a shift in the laboratory, there will be no meeting up with family and friends. This is a difficult and stressful time on many levels; we all too aware of the risks for some people of contracting the virus but for many the social and emotional trauma will be almost as difficult. I despair at some of the ghastly scaremongering "messages from a friend" that keep crawling around social media with dire warnings of social collapse and lonely deaths. This is not helpful at a time when anxiety levels are already heightened.

This brings me back to the approach taken by the Institute to this unprecedented health crisis; the constant stream of good, encouraging, sensible communications that are coming from our organisation says much about our profession – a profession to which I am proud to belong. I'd like to finish with a personal thanks to all our members in pathology for all you are doing, it does not go unnoticed and is very much appreciated.



Sarah May
Deputy Chief Executive

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

INSTITUTE OF BIOMEDICAL SCIENCE
12 Coldbath Square
London, EC1R 5HL
United Kingdom
+44 (0)20 7713 0214
+44 (0)20 7837 9658
Email: mail@ibms.org
Web: www.ibms.org

PRESIDENT
Allan Wilson CSci FIBMS

CHIEF EXECUTIVE
Jill Rodney

DEPUTY CHIEF EXECUTIVE
Sarah May CSci FIBMS

EXECUTIVE HEAD OF EDUCATION
Alan Wainwright CSci FIBMS

EXECUTIVE HEAD OF MARKETING AND MEMBERSHIP
Lynda Rigby

HEAD OF COMMUNICATIONS
Dan Nimmo

EDUCATION AND TRAINING
education@ibms.org

EXAMINATIONS
examinations@ibms.org

MEMBERSHIP
mc@ibms.org

CHARTERED SCIENTIST
chartered@ibms.org

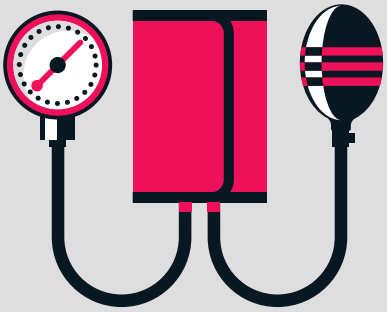
FOLLOW THE INSTITUTE

Join us on **facebook.com/biomedicalscience**

Follow us on Twitter **@IBMScience**

Find us on **LinkedIn**

SCIENCE NEWS IN NUMBERS

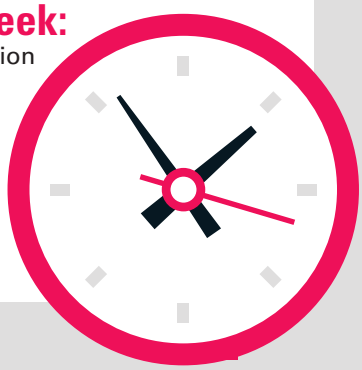


HYPERTENSION AND WORKING LONG HOURS

Working 49+ hours each week:
70% greater likelihood of masked hypertension
66% greater likelihood of sustained hypertension.

Working 41-48 hours each week:
54% greater likelihood of masked hypertension
42% greater likelihood of sustained hypertension.

These statistics come from a **Canadian study of 3500 white-collar employees**. They are in comparison with colleagues who worked fewer than 35 hours a week.



People with high blood pressure who take all their anti-hypertensive medication in one go at bedtime have **significantly lower risk of death or illness** caused by **heart or blood vessel problems**, compared to those who take their **medication in the morning**, according to new research.

When they looked at individual outcomes, they found risk of:

66% **Death** from heart or blood vessel problems was reduced by **66%**

44% **Myocardial infarction** was reduced by **44%**

40% **Coronary revascularisation** was reduced by **40%**

42% **Heart failure** was reduced by **42%**

49% **Stroke** was reduced by **49%**.

25%

Funding drop: Cancer Research UK expects to see its fundraising income decline by up to 25% in the next financial year as a direct result of the COVID-19 coronavirus pandemic. Many other charities expect similar drops.

Stents vs medication
New US research shows stents and surgery are no better than medication and lifestyle changes at reducing risk.

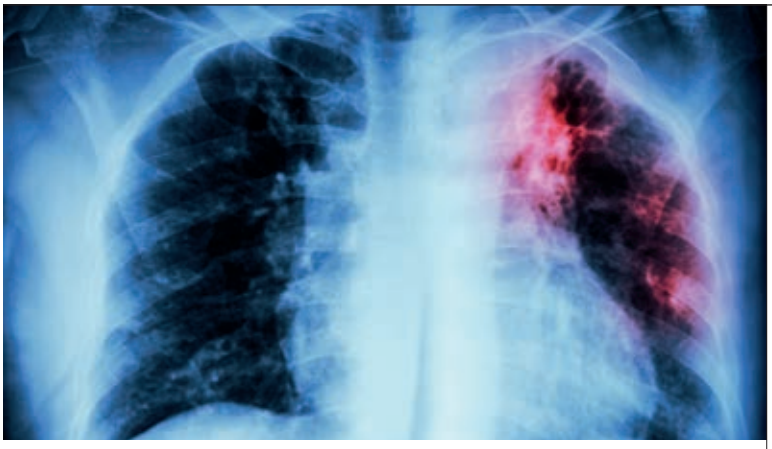
A trial followed more than 5000 patients with **stable heart disease and moderate to severe heart disease** for a median of 3.2 years.

Among those who had **invasive procedures, 145 died**, compared to **144 who received medication alone**.

100,000

It is estimated that every year, over 100,000 human deaths can be attributed to snakebite.

These are inflicted in self-defence when snakes feel threatened by encroaching humans. However, a new piece of research concludes that **snake venom did not evolve as a defence mechanism.** It reveals that **surprisingly few** venomous snake bites cause immediate pain, implying that the venom has **not evolved for a defensive primary purpose.**



SCIENCE NEWS

CELL BIOLOGY

GIANT CAVITY IN KEY TUBERCULOSIS MOLECULE

Scientists have discovered a strange new feature of a protein that is thought to be important in the development of tuberculosis.

The protein contains a "huge" interior pocket, the likes of which has never before been seen. It appears capable of passing a wide range of other molecules into the bacterial cell.

Cornelius Gati, a structural biologist who worked on the study, said they discovered the pocket while investigating the role this "transporter protein" on the surface of tuberculosis bacteria plays in sucking up vitamin B12 from surrounding cells.

It was widely thought that transporter proteins that import molecules into cells tend to be quite specialised, with structures that are tailored to grab onto particular molecules and move them into cells.

This one, Gati found, was a generalist that could, in principle, bring in small nutrients, larger molecules like vitamin B12, or even some antibiotics.

In theory, the new findings could lead to new ways to treat tuberculosis, but for the moment Gati and colleagues are trying to get a better handle on what the protein can and cannot transport.

"We've never seen anything like this before," Gati said. "It doesn't really make sense."

→ go.nature.com/2woONU2

COMPUTATIONAL BIOLOGY

New genetic cell insights

Researchers have developed the first computational model of a human cell and simulated its behaviour for 15 minutes.

This is the longest time achieved for a biological system of this complexity.

In a new study, simulations reveal the effects of spatial organisation within cells on some of the genetic processes that control the regulation and development of human traits and some human diseases.

The study, which produced a new computational platform that is available to any researcher, is published in the journal *PLOS Computational Biology*.

Zhaleh Ghaemi, study lead author, said: "This is the first programme that allows researchers to set up a virtual human cell and change chemical reactions and geometries to observe cellular processes in real time."

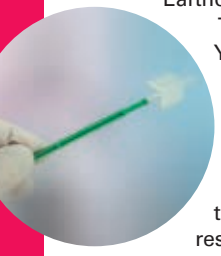
To test the platform the team performed simulations of RNA splicing – one of the most complex cellular processes.

→ bit.ly/2JNlei6

CERVICAL SCREENING

"DISASTER LEADS TO REDUCTIONS IN CANCER SCREENING"

Cervical cancer screening rates in Japan were significantly affected in the years following the devastating Great East Japan Earthquake of 2011.



Tohoku University's Yasuhiro Miki, who specialises in disaster obstetrics and gynaecology, was one of the scientists researching the issue.

He said: "Conflicts and disasters, and the social isolation that often follows, have a major impact on healthcare and lead to delays in the diagnosis and treatment of cancers."

On 11 March 2011, Miyagi Prefecture in eastern Japan experienced a 9.0 magnitude earthquake, followed by a destructive tsunami that affected its coastal areas.

Miki and colleagues examined how the earthquake affected cervical cancer screening rates in the area.

In the five years after the 2011 disaster, cervical cancer screenings dropped by more than 3% in four areas of Miyagi Prefecture.

Across Japan, approximately 15 women per 100,000 people are affected by cervical cancer.

This rate is higher than that in countries such as the US (6.5) and South Korea (8.4), and similar to that in India (14.7) and the Philippines (14.9).

Also, fewer than 1% of girls in Japan have received the human papillomavirus vaccine, which protects against cervical cancer.

This means that cervical cancer screening is of particular importance for early detection and diagnosis.

Even so, cervical cancer screening rates are lower in Japan compared to other countries, such as the UK.

→ bit.ly/2woRmW8

MEDICAL IMAGING

"AI RESEARCH COULD POSE RISK FOR PATIENTS"

Many studies claiming that artificial intelligence (AI) is as good as, or better than, human experts at interpreting medical images are of poor quality and potentially exaggerated.

The claim is published in *the BMJ*, in a paper that argues this could pose a risk for the "safety of millions of patients".

The findings raise concerns about the quality of evidence underpinning many of these studies and highlight the need to improve design and reporting standards.

AI is an innovative and fast-moving field with the potential to improve patient care and relieve overburdened health services.

Deep learning is a branch of AI that has shown particular promise in medical imaging.

The volume of published research on deep learning is growing, and some media headlines that claim superior performance to doctors have fuelled hype for rapid implementation.

However, the methods and risk of bias of studies behind these headlines have not been examined in detail, it is claimed.

To address this, a team of researchers reviewed the results of published studies over the past 10 years, comparing the performance of a deep-learning algorithm in medical imaging with expert clinicians.

They found just two eligible randomised clinical trials and 81 non-randomised studies. Of the non-randomised studies, only nine were prospective (tracking and collecting information about individuals over time) and just six were tested in a "real world" clinical setting.

The average number of human experts in the comparator group was just four, while access to raw data and code (for independent scrutiny of results) was limited.

→ **bit.ly/2JJbEfR**

IMAGES: ISTOCK/SHUTTERSTOCK

WHAT'S HOT AND WHAT'S NOT

HOT

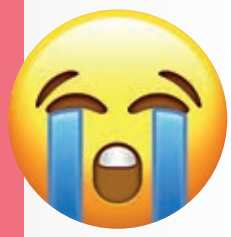
ULTRASOUND

Researchers at Columbia Engineering have used an ultrasound technique they pioneered a decade ago (electromechanical wave imaging) to accurately localise atrial and ventricular cardiac arrhythmias in patients.

HOT

TEARS

A new study found that the risk of COVID-19 transmission through tears is low, as no evidence was found of the virus in the tears of infected patients.



HOT

FEMALES

A new study shows that the average female wild mammal lives 18.6% longer than her male counterpart. In humans, the difference is 7.8 %.

NOT

ASPIRIN

Taking low-dose aspirin once a day does not reduce the risk of thinking and memory problems caused by mild cognitive impairment or probable Alzheimer's disease, a study had found.

NOT

TRANS FATS

Japanese researchers have uncovered a molecular link between some trans fats and a variety of disorders, including cardiovascular and neurodegenerative diseases.

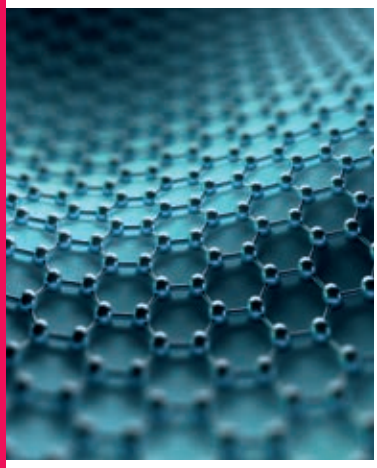
NOT

SALT

A high-salt diet is not only bad for blood pressure, but also for the immune system, concludes a new study.

BIOENGINEERING

Crumpled graphene for cancer detection



Graphene-based biosensors could usher in an era of liquid biopsy for detecting DNA cancer markers circulating in a patient's blood or serum.

Current designs need a lot of DNA, but a new study finds that crumpling graphene makes it more than ten thousand times more sensitive to DNA by creating electrical "hot spots".

The discovery was made by researchers at the University of Illinois at Urbana-Champaign.

Crumpled graphene could be used in a wide array of biosensing applications for rapid diagnosis, the researchers said.

Study leader Rashid Bashir, Professor of Bioengineering, said: "This sensor can detect ultra-low concentrations of molecules that are markers of disease, which is important for early diagnosis.

"It's very sensitive, it's low cost, it's easy to use, and it's using graphene in a new way."

While the idea of looking for telltale cancer sequences in nucleic acids, such as DNA or its cousin RNA, isn't new, this is the first electronic sensor to detect very small amounts, such as might be found in a patient's serum, without additional processing.

→ **go.nature.com/2Rdu5xB**

GENE THERAPY

MORE EFFECTIVE STEM CELL TRANSPLANT

Scientists have developed a new way to make blood stem cells present in the umbilical cord "more transplantable".

A University College London team said the finding could improve the treatment of a wide range of blood diseases in children and adults.

Blood stem cells, also known as haematopoietic stem cells (HSCs), generate every type of cell in the blood (red cells, white cells and platelets), and are responsible for maintaining blood production throughout life.

When treating certain cancers and inherited blood disorders, it is sometimes necessary to replace the bone marrow by allogeneic stem cell transplantation, which involves using stem cells from a healthy donor.

The umbilical cord is a useful source of blood stem cells, and cord blood transplants lead to fewer long-term immune complications than bone marrow transplants. Although umbilical cord transplants have been used in young children for the last 30 years, most cord blood units contain insufficient HSCs to be suitable for older children

UNDER THE MICROSCOPE

This month: Plant-based diets

OK, I know what a plant-based diet is. Let's skip straight on to why it's been in the news.

A review that has been published states that a plant-based diet can help prevent and manage asthma, while dairy products and high-fat foods raise the risk.

Tell me about the research behind this review.

Scientists examined the evidence related to diet and asthma and found that certain foods – including fruits, vegetables, whole grains and other high-fibre foods – can be beneficial, while others – such as dairy products and foods high in saturated fat – can be harmful.

What else did they observe?

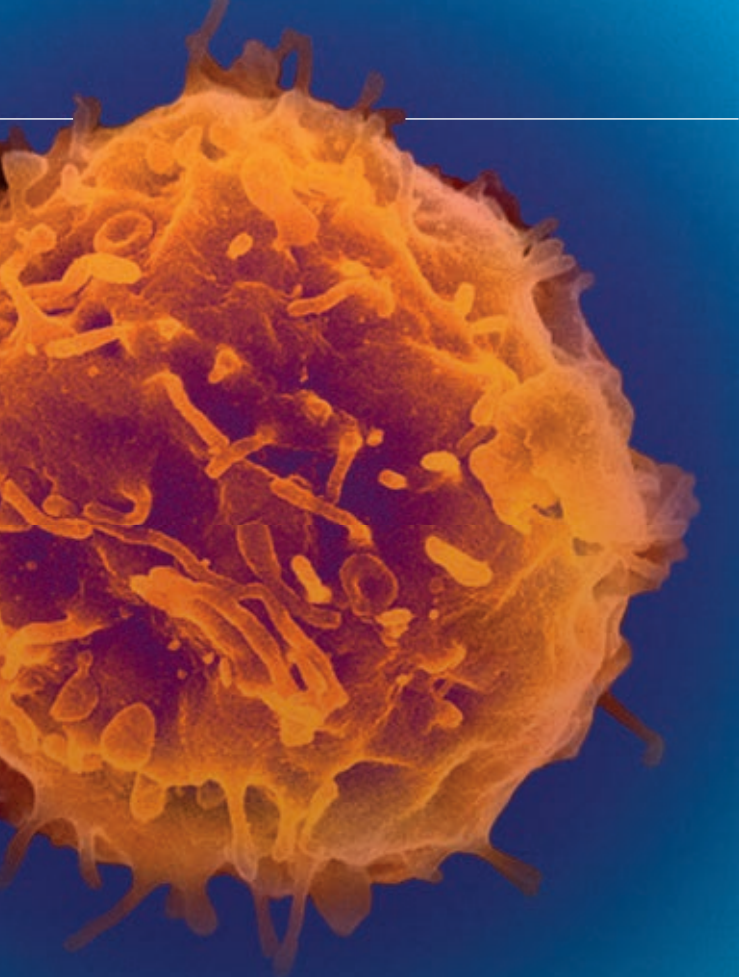
In another study, asthma patients adopted a plant-based diet for a year and saw improvements in vital capacity – a measure of the volume of air patients can expel. The authors suggest that a plant-based diet is beneficial because it has been shown to reduce systemic inflammation, which can exacerbate asthma. Plant-based diets are also high in fibre, which has been positively associated with improvements in lung function. The researchers also highlight the antioxidants and flavonoids found in plant foods, which may have a protective effect.

What about dairy and egg consumption having a negative impact?

One 2015 study found that children who consumed the most dairy and eggs had higher odds of developing asthma, compared with the children consuming the least. In another study, children with asthma were placed in either a control group, where they made no dietary changes, or in an experimental group where they eliminated dairy and eggs for eight weeks. After eliminating dairy, the experimental group experienced a 22% improvement in peak expiratory flow rate – a measure of how fast the children were able to exhale – while children in the control group experienced a 0.6% decrease.

High fat intake, consumption of saturated fat, and low fibre intake were also associated with airway inflammation and worsened lung function in asthma patients.

IMAGES: ISTOCK/SCIENCE PHOTO LIBRARY



and adults and 30% of all units contain too few even for the youngest children, and go to waste.

The study shows how a protein called NOV/CCN3, which is normally found at low levels in the blood, can be used to rapidly increase the number of HSCs in single umbilical cord blood units that are capable of transplantation.

This finding potentially opens the door to units that would otherwise be discarded being made available for patients of all ages.

→ **bit.ly/2JlANrj**

ECOLOGY

NEW ANTIBIOTIC RESISTANCE GENE

Aminoglycoside antibiotics are critically important for treating several types of infections with multi-resistant bacteria.

A completely new resistance gene, which is likely to counteract the newest aminoglycoside drug, plazomycin, was recently discovered by scientists in Gothenburg, Sweden.

The bacterial gene the team discovered in river sediment from India does not resemble any known antibiotic resistance gene.

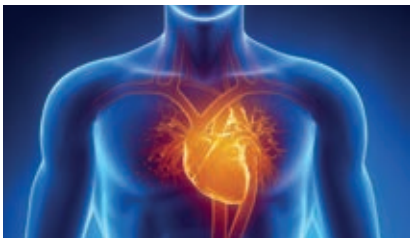
But when the scientists compared its DNA sequence to already published bacterial DNA sequences, they found that it was already present in several pathogens, including *Salmonella* and *Pseudomonas*, from the USA, China and Italy. Until now, no one had realised that it was a resistance gene.

The research team has named the gene "*gar*".

→ **bit.ly/39Mcrrf**

BIOTECHNOLOGY

CURATIVE TREATMENT FOR HEART DISEASE?



Researchers trying to turn off a gene that allows cancers to spread have made a surprising U-turn.

By making the gene overactive and functional in the hearts of mice, they have triggered heart cell regeneration. Since adult hearts cannot usually repair themselves once damaged, harnessing the power of this gene represents progress towards the first curative treatment for heart disease.

Dr Catherine Wilson, a researcher in the University of Cambridge's Department of Pharmacology, who led the study, said: "This is really exciting because scientists have been trying to make heart cells proliferate for a long time.

"None of the current heart disease treatments are able to reverse degeneration of the heart tissue – they only slow progression of the disease. Now we've found a way to do it in a mouse model."

→ go.nature.com/3clm5m8

COVID-19

CONVALESCENT PLASMA THERAPY

A US team of Johns Hopkins experts has created a clinical guidebook to help hospitals and medical centres rapidly scale up their ability to deliver so-called convalescent plasma therapy, which leverages immune system components found in the plasma portion of blood from people who have recovered from COVID-19.

Evan Bloch, an Associate Professor of Pathology at the university's School of Medicine, is part of the team that is working on convalescent therapy.

He said: "We've received many inquiries from healthcare providers looking to ramp up their ability to deliver this therapy.

"There is historical precedent for its use to prevent and treat viral illness. However, during the chaos of an epidemic, the therapy is often deployed without rigorously studying its effects. Carefully conducted studies are critically needed to understand which people are most likely to benefit from this therapy and how best to apply it to optimise that benefit."

The paper details how to deploy convalescent plasma, and is aimed to help people worldwide who are preparing to use this therapy against COVID-19.

The guidebook has been published online in *The Journal of Clinical Investigation*.

→ bit.ly/2XChZIz

NEUROLOGY

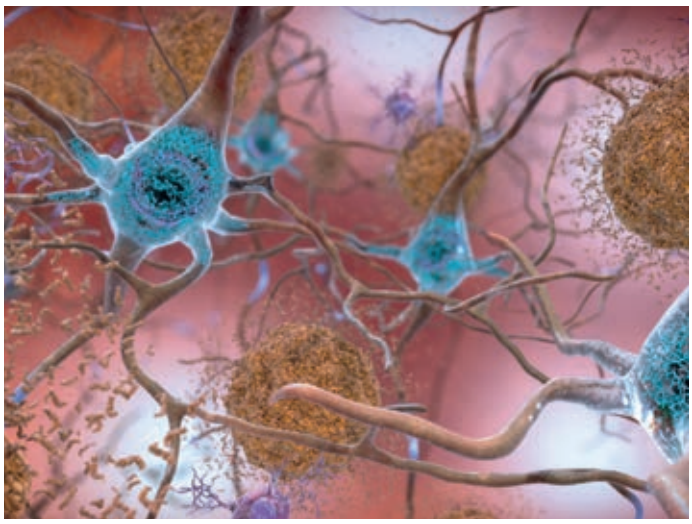
GENE VARIANT STAVES OFF ALZHEIMER'S

People with a gene variant that puts them at high risk of Alzheimer's disease are protected from its debilitating effects if they also carry a variant of a completely different gene, Stanford University School of Medicine investigators report in a new study.

Their findings suggest that a substantial fraction of the estimated 15% of people carrying the high-risk gene variant are protected to some degree from Alzheimer's disease by a variant of the other gene.

The findings may help drug developers better identify clinical trial participants and treatments for what, despite billions of dollars spent in pursuit of effective therapies, remains a disease without a cure.

→ stan.md/2xnEjF3



IMAGES: ISTOCK/SHUTTERSTOCK/THE NATIONAL INSTITUTE ON AGING/NATIONAL INSTITUTES OF HEALTH

TECH NEWS

THE NATIVE ANTIGEN COMPANY

ANTIGEN COLLAB

OXGENE and The Native Antigen Company have announced a collaboration to scale up production of COVID-19 reagents.

They will do so by combining OXGENE's proprietary adenoviral protein machine technology with The Native Antigen Company's antigen development expertise. They will aim to scale their antigen manufacturing to deliver proteins for the development of diagnostics and vaccines.

→ **thenativeantigencompany.com**

PROMEGA

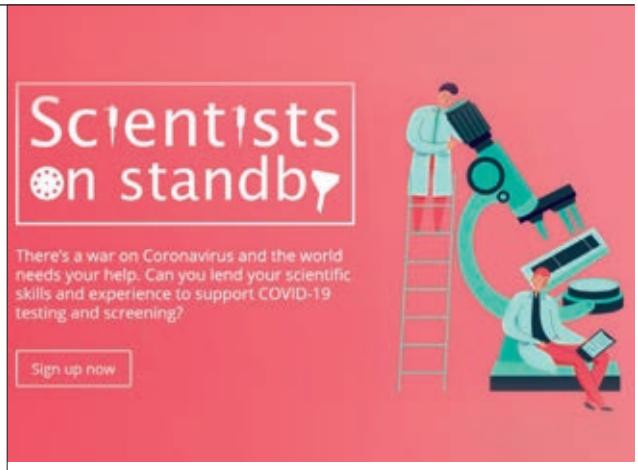
US APPROVAL

Promega Corporation's GoTaq Probe 1-Step RT-qPCR System is now in a Centres for Disease Control and Prevention COVID-19 diagnostic protocol for emergency use.

The Promega tool is an approved master mix option for the CDC's 2019-Novel Coronavirus Real-Time RT-PCR Diagnostic Panel, available through emergency use authorisation.

In a March 30 letter, the FDA granted approval of an amendment to the CDC's diagnostic COVID-19 assay.

→ **promega.co.uk**



BIOSTRATA

SCIENTISTS ON STANDBY PORTAL

BioStrata, a specialist life science marketing agency, has launched Scientists on Standby – a new portal to support the recruitment of qualified scientists and researchers who could volunteer their time and expertise in the sample testing and screening of the coronavirus.

The portal will provide government bodies and diagnostic testing laboratories with a database of UK-based volunteers specialising in reverse transcription-polymerase chain reaction, immunoassays and good laboratory practice, all grouped by location for easy regional allocation.

→ **scientistsonstandby.com**

THE BIG QUESTION

THIS MONTH WE ASK

"How do you think public approaches to health and wellbeing will change when the current pandemic is over?"

Sue Alexander

Pathology Services Manager
The Royal Marsden NHS Foundation Trust

I would like to think that there will be a far greater awareness among the British people that pandemics and disasters do not happen far away, or mostly to other people, like the 2004 tsunami, the Ebola outbreaks and the Fukushima 2011 nuclear power plant disaster.

This current pandemic has woken people up to the fact that wealthy, industrialised nations with modern healthcare systems can be at the mercy of an infection and that these healthcare systems can themselves become overwhelmed. I'd also like to think that the impact of the spread of the infection and the escalating approaches by government towards measures designed to limit this will remain in people's minds for a long time to come.

I hope that everyone will become more aware of the need for continued good hygiene, respectful of each other's personal space, understand the issues that the NHS is up against and perhaps remember that biomedical scientists are key workers in the testing processes.

The impact of the infection should leave a serious impression on the psyche of the nation, making us aware of the freedoms we always took for granted and encourage the government to rethink how the NHS is funded.

There is clearly a big public "thank you" for NHS workers and all the other key workers and it should be the case that people now understand that their behaviour can affect public health issues and contribute to maintaining a more healthy society going forwards.

IMAGE: IKON

Colin Mudd

Higher Specialist Biomedical Scientist
Nottingham University Hospitals NHS Trust

The current situation regarding the COVID-19 pandemic has certainly focused the public's opinion on healthcare matters. The contribution to the wellbeing and health of the nation by the NHS has been widely appreciated.

Finally, the magnificent machinery of the NHS, with the myriad parts that make up the whole, is at the forefront of everyone's minds and people now realise what is needed to make it work effectively. All the NHS workers, frontline clinical and nursing staff, support services and laboratory staff have had significant parts to play.

A great hope is that the public will realise their contribution to the health of the nation from following government recommendations – they can positively contribute to disease control sometimes by simply doing nothing, by staying at home.

I wonder once the pandemic is over if the public will become complacent, or will have learnt a significant lesson from the death toll and the changes that have occurred to all of our lives in bringing the pandemic under control.

Now is not the time for a business-as-usual, stiff-upper-lip attitude, but rather a time for recollection, reflection and re-evaluation of all that we hold dear.

To borrow from past world-changing events... perhaps our watchwords might be "lest we forget". People have died so that we might live. That sounds melodramatic – perhaps trite – but is absolutely the case. We must all learn and improve from this dreadful pandemic.

Simon Parker

Clinical Market Manager
Roche Diagnostics Limited

Life will never be the same again. We face a major hangover after this pandemic – family tragedy, jobs lost and the country on its knees. But, strangely, I sense new shoots of hope for humanity and a fresh bewildering sense of purpose. Friendship is a powerful antidote and within both my organisation and neighbourhood, I have been amazed just how many people I didn't know before, that I now know on various mobile apps.

My company has been adapting to future ways of working, but no one prepared us for sudden isolation. On our own we may be, but online we are many and together we are strong.

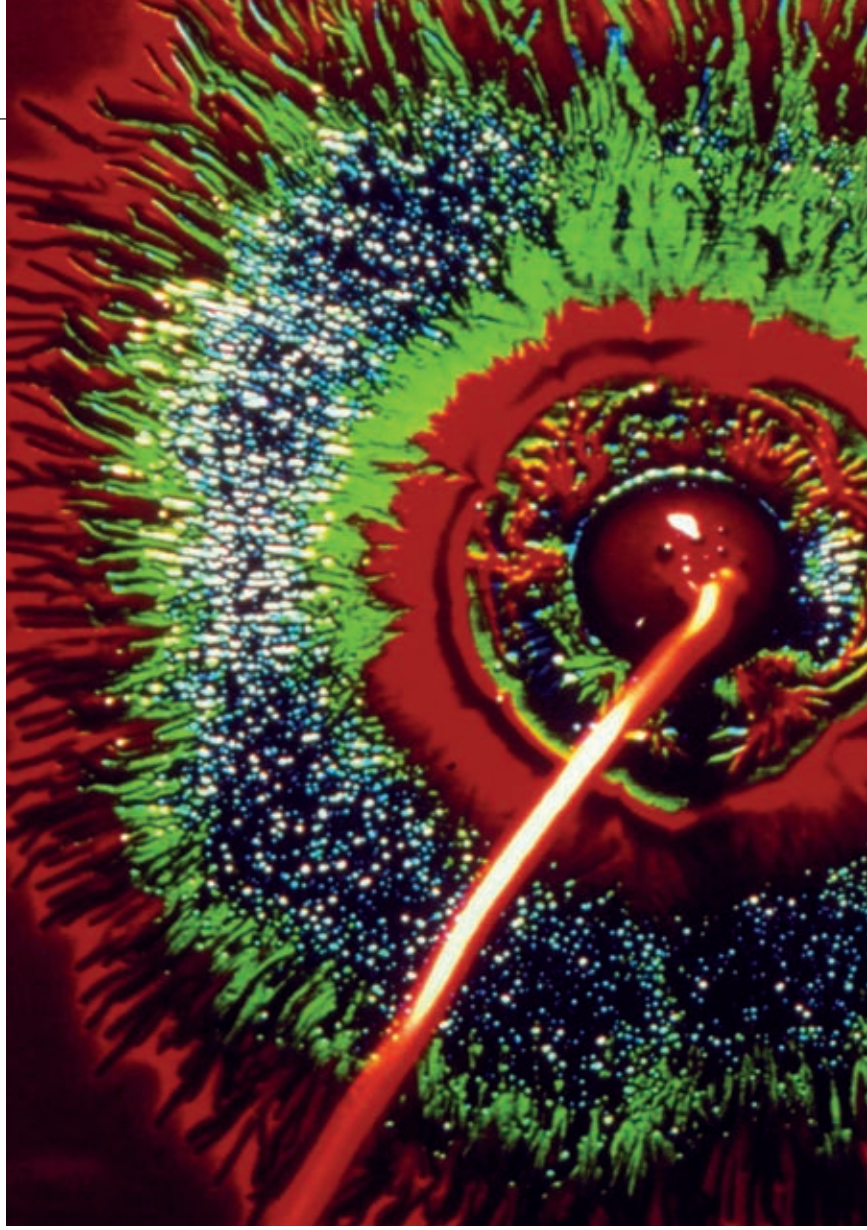
This is how I see the future. Adapting to home working with digital technology, saving the environment and saving one of the most precious things – time.

COVID-19 has certainly put diagnostics on the map and I hope we will see a drive towards prevention and the value of public health over cure.

So, what else? A renewed focus on walking and fresh air, for mental health and wellbeing. My family has started baking and enjoying the challenge of just one shop every two weeks. Being at home has also meant us coming together more.

Let's touch on the negatives – we will always be looking over our shoulders for the next outbreak; it's not going away but, like many life lessons, next time we will be more prepared and will lose less lives.

We talked as a family about this question and I hope these few words reflect on their views as much as mine. I know many of my colleagues would also agree.



THE CANCER TEST OF THE FUTURE?

The efforts of cancer research scientists around the world continue to throw up new possibilities that could give clinicians the edge in the fight against the disease. The latest is a blood test that, it is claimed, may be able to detect more than 50 different types of cancer.

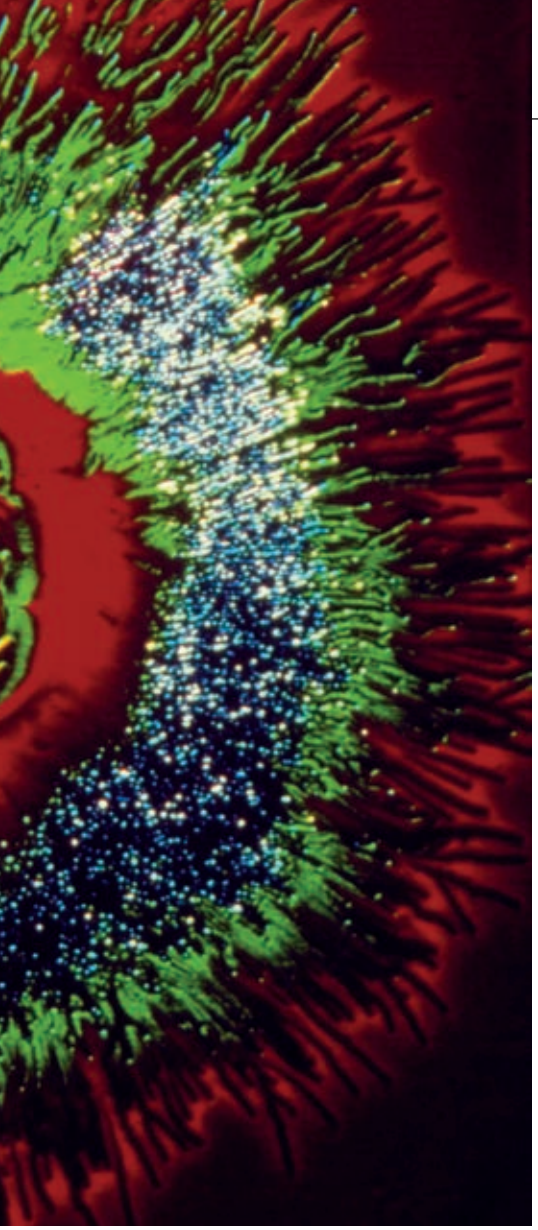
Published in the *Annals of Oncology*, "Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA" is a multinational piece of research involving, among others, scientists from The Francis Crick Institute, University College London, and the Dana-Farber Cancer Institute and Harvard Medical School in the US.

Their work has its roots in a previous breakthrough a few years ago, when small pieces of DNA were found in the bloodstream, as Dr Michael Seiden, President of the US Oncology Network, and one of the lead authors of the research, explains: "This DNA, which is normally in the centre of the cell, had broken into much smaller pieces and floated out into the blood, almost like when you put the trash out to be recycled. This was discovered in pregnant women. Some DNA from the baby could also be found in the mother's womb. So by looking at the chromosome you could detect the sex of the baby. With a little more sophistication, you could determine whether the baby was carrying certain genetic abnormalities. A foetal monitoring industry grew up around this."

Thousands of pregnant women were tested this way, though occasionally researchers would come across untypical bits of DNA. "Eventually one of these advisors noticed that this DNA looked just like the kind of abnormalities you would find in cancer cells," says Seiden. At first, the response was scepticism – the blood was from pregnant women, not cancer patients. "But they went back to these women and sure enough, they did have cancer. It was this observation that alerted scientists that even if the cancer was relatively modest in size and confined to an organ, some of these cells would still spontaneously die and shed their DNA into blood."

Workable tests

Suddenly, the race was on to find a way to turn this new knowledge into a practical, workable test, though several questions needed answering first. "What sort of snippets of DNA should you be looking for?" asks Seiden. "How would you optimise an assay, and how could you come up with something that was specific enough that could work as a



IMAGES: SHUTTERSTOCK/SCIENCE PHOTO LIBRARY

"Suddenly, the race was on to find a way to turn this new knowledge into a practical, workable test"

screening tool that would accurately record a normal or negative result for the vast majority of people who did not have cancer at any given time?"

The team that initially wrestled with this problem included bio-informatics experts, mathematicians, computer scientists and DNA sequencing specialists. They had to decide which path to pursue. "One was to collect and sequence every bit of DNA we could find. In other words, we have no idea what we're looking for, so we're going to evaluate everything. A second approach was to collect just the DNA related to specific types of cancer. That's like looking for just one item. And the third approach was based on turning certain genes on or off by a process called methylation. Through a few tricks in chemistry you can identify and sequence only the methylated DNA.

The next step was to see which of the tests worked best by trying each of them on blood samples from cancer patients. "All three went pretty well," says Seiden. "There weren't major differences, but the methylation test was slightly more sensitive and specific. It was also less technically demanding, so if you were aiming to repeat this for millions of people at a lower price point and as quick as possible, it was probably the easiest to get done."

Not the perfect test

Following this long process of test building, the methylation method was tried on another large group of patients known to have cancer, and a second group believed to be free from the disease. In those people with the disease, could the test accurately pinpoint the location of the cancer? Beyond that, could it detect a faint signal of the disease before it had progressed to an advanced stage?

"The paper shows that the test is extraordinarily sensitive at detecting advanced cancer. In terms of patients with very early cancers, it only picked out one in five. However, it did considerably better with a certain subset. It did well with oesophageal, pancreas and lung cancers, but less well with breast and kidney cancer. For the cancers that in general are most lethal, many of which don't currently have screening tests, it has a 40% plus chance of detecting them even at an early stage."

Where does that leave the test? "My guess is that this won't be the perfect blood test that means you no longer need anything else," says Seiden. "But I do think it has the opportunity to play a couple of roles. First, it can screen for cancers that we don't have any tests for. Second, as a simple blood test, it doesn't have some of the challenges and risks that, say, colonoscopy and things like that have."

A period of fine-tuning has now started, with a further study enrolling patients for lung cancer screening, and another working with patients who simply feel ill. "It's not clear why they don't feel well, but we are giving them the blood test to see if it might indicate an undiagnosed cancer. This study is working with several thousand patients and hopefully we'll have some results either later this year or early next year."

Until then, it remains to be seen whether the methylation test has a potential clinical role. "We don't have enough data yet but part of the goal is to give clinicians, epidemiologists and healthcare policymakers a body of evidence to look at so they can make decisions about where this test might fit in a population cancer screening strategy." BMS

DR MICHAEL SEIDEN

- ✔ **1976-80:** BA Chemistry, Oberlin College, Ohio
- ✔ **1980-86:** MD PhD Immunology, Medicine, Washington University, St Louis
- ✔ **1994-2007:** Chief of Clinical and Translational Cancer Research, Massachusetts General Hospital
- ✔ **2007-13:** CEO, Fox Chase Cancer Centre
- ✔ **2013-18:** Chief Medical Officer, McKesson Specialty Health and the US Oncology Network

IN SEARCH OF A VACCINE

We look at the frontline of vaccine development and how and when immunity to COVID-19 may be a possibility.

On 10 April this year, a month after the World Health Organization announced that the COVID-19 outbreak could be considered a pandemic, the global death toll reached more than 100,000 people. Nearly two million cases of the disease have been confirmed worldwide. With nearly all regions of the world affected by the virus SARS-CoV-2, a novel type of coronavirus that first emerged in central China at the end of 2019, this can be considered the worst pandemic in the world's recent history.

Responding to the crisis

Research teams worldwide have been on the frontline since January 2020, supporting healthcare workers by working to design diagnostic tests, experiment treatment options and gather crucial information about the virus itself. Yet, despite the growth of the anti-vaccination movement in many countries around the world in recent years, it's the perspective of developing a safe and effective vaccine against the deadly disease that is crystallising all the hope. "Getting a safe and effective vaccine for COVID-19 would be a game-changer in this pandemic, protecting people against the disease, cutting down the number of deaths, and making measures, such as quarantine, unnecessary. Experts expect a vaccine to be ready in 12 to 18 months", says Gary Kobinger, Director of the Infectious Disease Research Centre at the Université Laval (Canada) and member of the Strategic and Technical Advisory Group for Infectious Hazards at the World Health Organization.

Although the timeline remains uncertain, vaccine development in response to COVID-19 is going at an unprecedented pace. On 11 January 2020, the genetic sequence of SARS-CoV-2, was published and shared with scientists worldwide. This marked the beginning of intense global R&D efforts to develop a vaccine against COVID-19, paving the way for the start of many vaccine trials in 2020. As of 8 April 2020, 115 vaccine candidates were being studied as part of the global COVID-19 vaccine R&D landscape. In total, 78 of these were confirmed as active, with 73 at exploratory or preclinical stages.

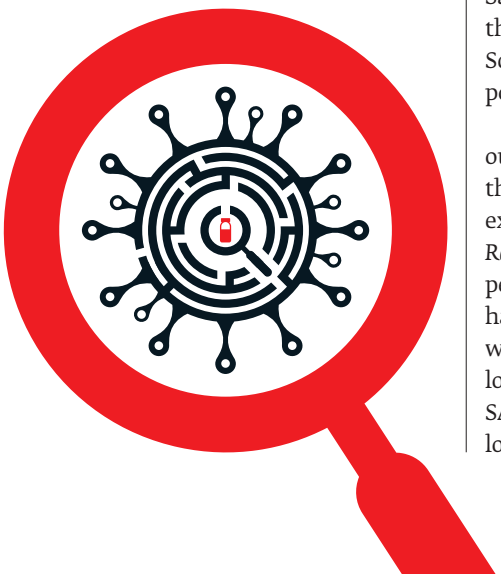
The most advanced vaccine candidate, the mRNA-1273 vaccine from US-based company Moderna Therapeutics, entered

phase 1 human clinical trials on 16 March 2020. Phase 2 clinical trials are expected to start in May. Most of the other advanced candidates are based in the US and in China and include Ad5-nCoV from CanSino Biologicals, INO-4800 from Inovio, LV-SMENP-DC and pathogen-specific aAPC from Shenzhen Geno-Immune Medical Institute. In other countries, research groups – such as the Jenner Institute at the University of Oxford – have announced that they would also go through the first phases of human testing before the end of the year.

The challenges of developing a vaccine

Designing a vaccine in under 18 months represents a considerable feat, considering that most vaccines take between five and 10 years to be developed. A number of challenges need to be addressed before a vaccine candidate is deemed safe and effective. Perhaps one of the biggest difficulties is the fact that SARS-CoV-2 remains elusive to researchers. In order to develop a safe and effective vaccine, interrogations surrounding the way the immune system responds not only to the virus, but to any potential vaccine too, first need to be addressed.

"We need to better understand the immune response before we can progress to successful vaccine development.



Studies looking at the type of coronavirus that can cause the common cold suggest that antibodies built against this virus don't last long in the body. This tells you that the immune response differs to what can be seen with other viruses. This is one of the reasons why a vaccine against SARS-CoV-2 may be difficult – it might be hard to elicit long-term immunity against this novel coronavirus," Sarah Pitt, microbiologist and professor at the School of Pharmacy and Biomolecular Science at the University of Brighton, points out.

Research from the 2002-04 SARS outbreak suggests immunity against the virus may not last long after a first exposure. A study published in *Annual Reviews of Immunology* showed that 10% of people who had been infected by the virus had lost the immunity they had built within 12 months. Understanding how long people who have been infected by SARS-CoV-2 are immune to it, and how long a vaccine candidate can elicit

protection, are key questions researchers are trying to solve in order to improve vaccine development. The yellow fever vaccine is considered one of the best vaccines in the world, because only one dose is needed to confer lifelong immunity, with few sideeffects. It is unclear whether sustaining a robust immune response in the long term with a COVID-19 vaccine will be possible.

Another source of concern for the teams working on vaccine development is how to avoid a phenomenon that seems to contradict our conventional understanding of vaccine science, and which has been observed since the 1960s, during vaccine trials for diseases such as dengue or SARS. Indeed, in some animal models or even in some human trials, those who had received a vaccine candidate and were later re-exposed to the virus paradoxically developed a more severe form of the disease. In other words, the vaccine-primed immune system, in some cases, malfunctions when the body is exposed to natural infection. Known as antibody-dependent enhancement (ADE), this reaction involves the virus leveraging antibodies to aid infection. Making sure that ADE is not happening in the context of the COVID-19 pandemic, and that none of the vaccine candidates currently tested against the disease trigger such a reaction, is a priority for research teams.

It is unclear if a robust, long-term immune response with a COVID-19 vaccine will be possible

For some experts, setting up human challenge models, which involves testing vaccine candidates in healthy human volunteers and then intentionally infecting them with an attenuated form of the virus under controlled conditions could provide useful information about the immune system's interaction with the virus. In the case of malaria vaccine research, for example, these models have allowed for more thorough vaccine efficacy testing and are informing rational vaccine development. Without knowing more about SARS-CoV-2 though, and without properly addressing safety concerns that participants may have

before taking part in this kind of research, these models may be difficult to set up. Animal models to start testing candidates will remain the norm.

Funding research

Financial concerns are also still on the table. Developing successful vaccines and using them for large-scale immunisation not only requires robust research but also support from the industry and appropriate funding. "Different factors can influence whether a vaccine will be developed or not, such as how many people are dying and whether it is a high-profile disease. There are financial considerations that are taken into account by pharmaceutical companies. Take polio for example – in the 1950s there was a lot of interest in getting a vaccine, and the US government secured funding for it, because the disease was affecting teenagers in the US and in Europe," Sarah Pitt says.

The virus that caused polio was identified in the early 20th century, but it took more than 40 years for vaccine trials to start. However, from the 1950s, the US government's financial involvement was crucial in the fight against the disease. In 1955, the inactivated poliovirus vaccine was introduced with massive support from the federal government. Federal funds were allocated to states in 1955 and 1956 to help them buy and administer the vaccine and, in 1960, Congress made an appropriation for a stockpile of the vaccine to be used in combating future polio epidemics.

In 1955, the inactivated poliovirus vaccine was introduced with massive support from the federal government

The scale of the current pandemic means that massive funding has already been allocated to vaccine research. However, it is crucial that this research be allowed to go on and that some vaccine candidates be allowed to go through different stages of clinical testing. When SARS appeared in China, about 20 years ago, investigations of potential vaccine candidates were conducted. However, before clinical trials could start, funding was cut short as SARS was no longer spreading, and there was reduced interest in developing a vaccine. Many researchers now believe that if candidate vaccines for SARS, or even for Middle East Respiratory Syndrome (MERS), had received clinical trial funding years ago, current research to develop a vaccine against COVID-19 would have been facilitated, with a lot of lessons learnt for the current pandemic.

FAST FACTS: VACCINE DEVELOPMENT

115
CANDIDATES
A total of 115 vaccine candidates were being studied as part of the global COVID-19 vaccine R&D landscape, as of 8 April.

5-10
YEARS
Most vaccines take between five and 10 years to be developed.

45
VOLUNTEERS
Initial human trials for mRNA-1273 featured 45 healthy adult volunteers aged 18 to 55 years, over approximately six weeks.

Identifying the right vaccine technology

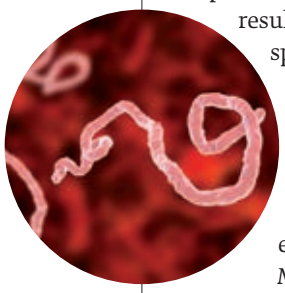
Despite the magnitude of the crisis, the vaccine development landscape for COVID-19 is particularly dynamic, with many different technology platforms being evaluated. This dynamism, and the innovation displayed by different research teams around the world, enables different approaches to be tested quickly, comparing their efficacy, in the hope of finding a successful vaccine candidate among them. Furthermore, developing and testing different technologies gives scientists more opportunities

to test and identify vaccine platforms that may be better suited for specific population subtypes (such as the elderly, immunocompromised patients and healthcare workers).

These different approaches include nucleic acid (such as the mRNA-1273 vaccine), peptide, viral vector recombinant protein, live attenuated virus and inactivated virus strategies. Some of the newest technologies are of particular interest to the scientific community. "Broadly speaking, we can divide these approaches into two groups – killed or live attenuated vaccines, and subunit vaccines that are designed using only specific parts of the virus, made with the newest technologies. These subunits have the clear advantage that they can't cause the disease, as opposed to attenuated vaccines, such as the polio vaccine that can cause an attenuated form of the disease," Gary Kobinger points out.

Learning from a previous crisis

Recent large-scale epidemics, such as the 2013-2016 Ebola epidemic in West Africa, are providing researchers with valuable lessons for managing the current crisis and conducting research in an emergency context. Research teams worldwide hope a vaccine could be ready in 18 months because that's the time it took to get a vaccine against Ebola. Working quickly but ethically and with high standards of quality, coordinating international efforts and developing innovative technology platforms have all been important features of the research world during the Ebola crisis, and will be even more important in the current pandemic.

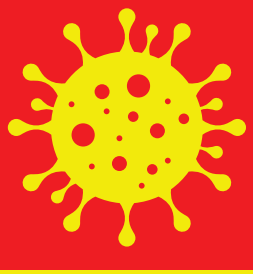


Gary Kobinger was a key scientist in the team working to create the Ebola vaccine and has conducted a lot of research work in the context of other epidemics, including the Zika outbreak. He believes some of the vaccine work done in these previous contexts can be useful in the fight against COVID-19. In fact, some teams are using some of the technology platforms investigated during Ebola to see if they could provide interesting clues to create a successful vaccine.

Working urgently to get a vaccine, and getting it done in less than 18 months, does not mean rushing through all the steps and forgetting safety and ethics rules, however. "A vaccine candidate needs to be tested not just for efficacy but also for safety; we don't want to rush the development of a vaccine just because there is panic caused by the epidemic, with the potential of worsening the situation with a poorly manufactured and poorly tested vaccine," Sarah Pitt warns.

There are ways to accelerate the pace of vaccine development without risking the safety of patients. Gary Kobinger explains: "The steps you need to follow in a clinical trial are always there, the question is how we can move through them faster. There are things that can be done, such as overlapping a phase 1 and a phase 2 trial, which means you start the phase 1 trial with the documentation for the phase 2 already in place, pending the results. Another way is to target specific subgroups, such as young adults, healthcare workers or the elderly. If you restrict the target population you may be able to go faster, because it makes the research easier to set up."

Many questions about the COVID-19 pandemic remain unanswered, and we still don't know exactly when a successful vaccine will be ready. Yet there's cause for optimism: all the research conducted today will prove useful in the future, not only to develop the future COVID-19 vaccine, but also to allow researchers to progress in their understanding of new technologies, advancing the development of subunit vaccines to protect us against future emerging viruses. BMS



TIMELINE: DEVELOPMENT OF THE PANDEMIC

31 DEC
China reported a cluster of cases of pneumonia in Wuhan. A novel coronavirus was eventually identified.

13 JAN
Officials confirm a case of COVID-19 in Thailand – the first recorded case outside of China.

31 JAN
Two Chinese nationals staying in a hotel in York became the first confirmed cases of COVID-19 in the UK.

28 FEB
The earliest documented transmission within the UK appeared to take place.

1 MAR
COVID-19 was detected in England, Wales, Northern Ireland and Scotland.

11 MAR
The WHO declared the outbreak a pandemic.

20 MAR
UK restaurants, pubs, clubs, and indoor sport and leisure facilities were ordered to close.

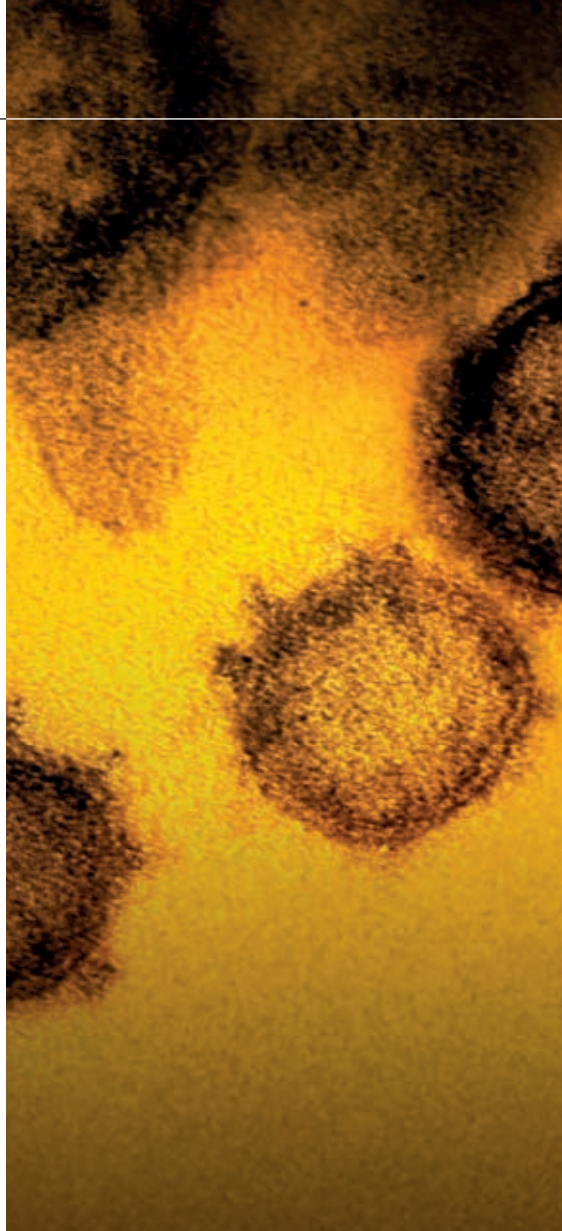
5 APR
Boris Johnson was hospitalised after testing positive for COVID-19.

12 APR
Boris Johnson left hospital to recuperate at Chequers.

16 APR
Dominic Raab, deputising for Boris Johnson, announced the UK lockdown would stay in place until at least 7 May.

AN EDUCATED GUESS?

Adrian Esterman, Chair of Biostatistics at the University of South Australia's Cancer Research Institute, asks: "Can we believe the statistics about COVID-19?"



Well, in brief, probably not. The reason is that every single statistic that is quoted is either an educated guess, or has a heap of caveats attached to it, which are usually barely (or never) mentioned. Let's look at some of examples of the commonly used rates, parameters and statistics that keep appearing in articles about COVID-19.

The epidemic curve

The epidemic curve is actually a bar chart showing the number of newly diagnosed cases of COVID-19 on the *y* or vertical axis, and the date or days from first diagnosed case on the horizontal or *x*-axis. Sounds simple? Let's assume that the date is reasonably accurate. The number of newly diagnosed cases is highly dependent on two factors: (a) the accuracy of the diagnostic test; and (b) the number of people tested each day. With respect to accuracy, some tests use nasal swabs, others buccal swabs, and now we are just about to get fingerprick testing for blood samples. If more than one of these is used for the same person, then it is quite possible, and even likely, that they will disagree.

As for testing rates, if the probability of infection is spread evenly across the population, then if we double the number of tests, we double the number of diagnosed cases. Therefore, epidemic curves are really only useful if the testing criteria and rate are steady across the course of the epidemic. We can then interpret the patterns correctly. For example, if we see a downward trend of the initially exponential growth of cases, then it is likely to be true.

The case fatality rate

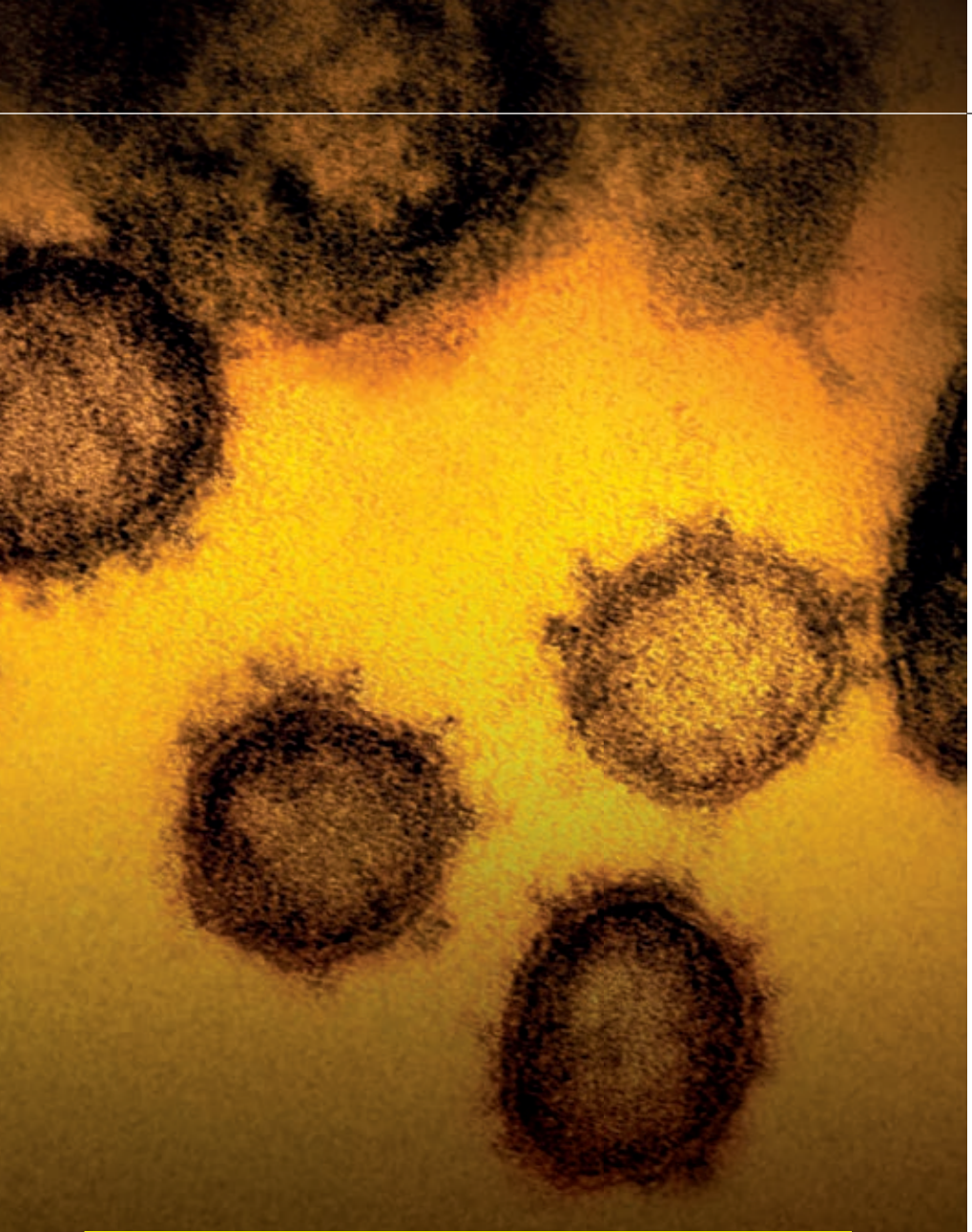
This is the number of deaths from COVID-19 over a given period divided by the number of diagnosed cases. The numerator – the number of deaths – is likely to be reasonably accurate. However, the denominator – the number of diagnosed cases – suffers the same fate as the epidemic curve; it is very dependent on the testing rate. For example, to the right is a graph of case fatality rate by testing rate.

By and large, countries such as Australia and Germany with the highest testing rates also have the lowest case fatality rates. Because of this, it is likely that the global case fatality rate is around 1% or just over.

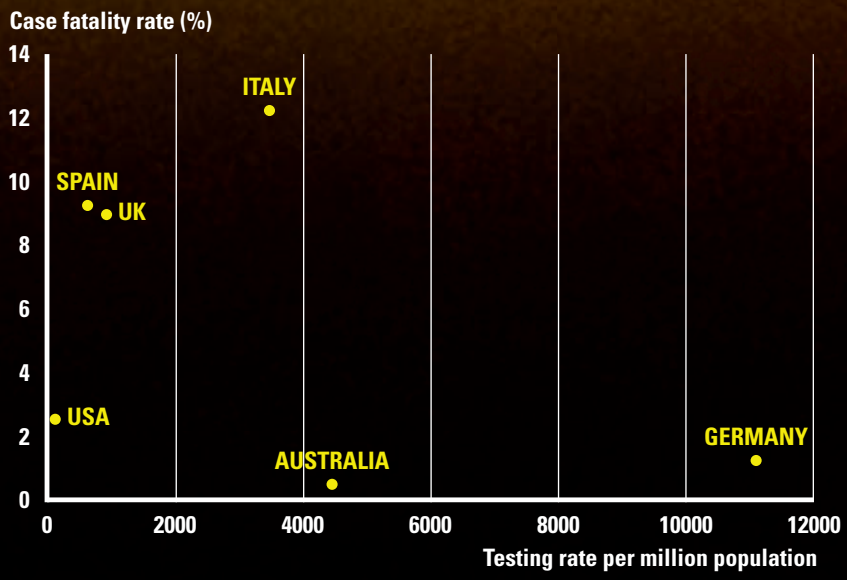
Incubation period

This is the time from first exposure to the infection until the onset of symptoms. Sometimes the time of exposure is relatively easy to sort out – for example, you went to a meeting at which someone was infected. However, especially for community-acquired infections, we have no idea when exposure occurred. As for

IMAGES: SCIENCE PHOTO LIBRARY



PLOTTING OUT COVID-19: CASE FATALITY RATES AND TESTING RATES



the onset of symptoms, many infected people are asymptomatic. Current estimates of the incubation period are from one to 14 days, with a median of five days, which are obtained from known exposures and symptomatic individuals.

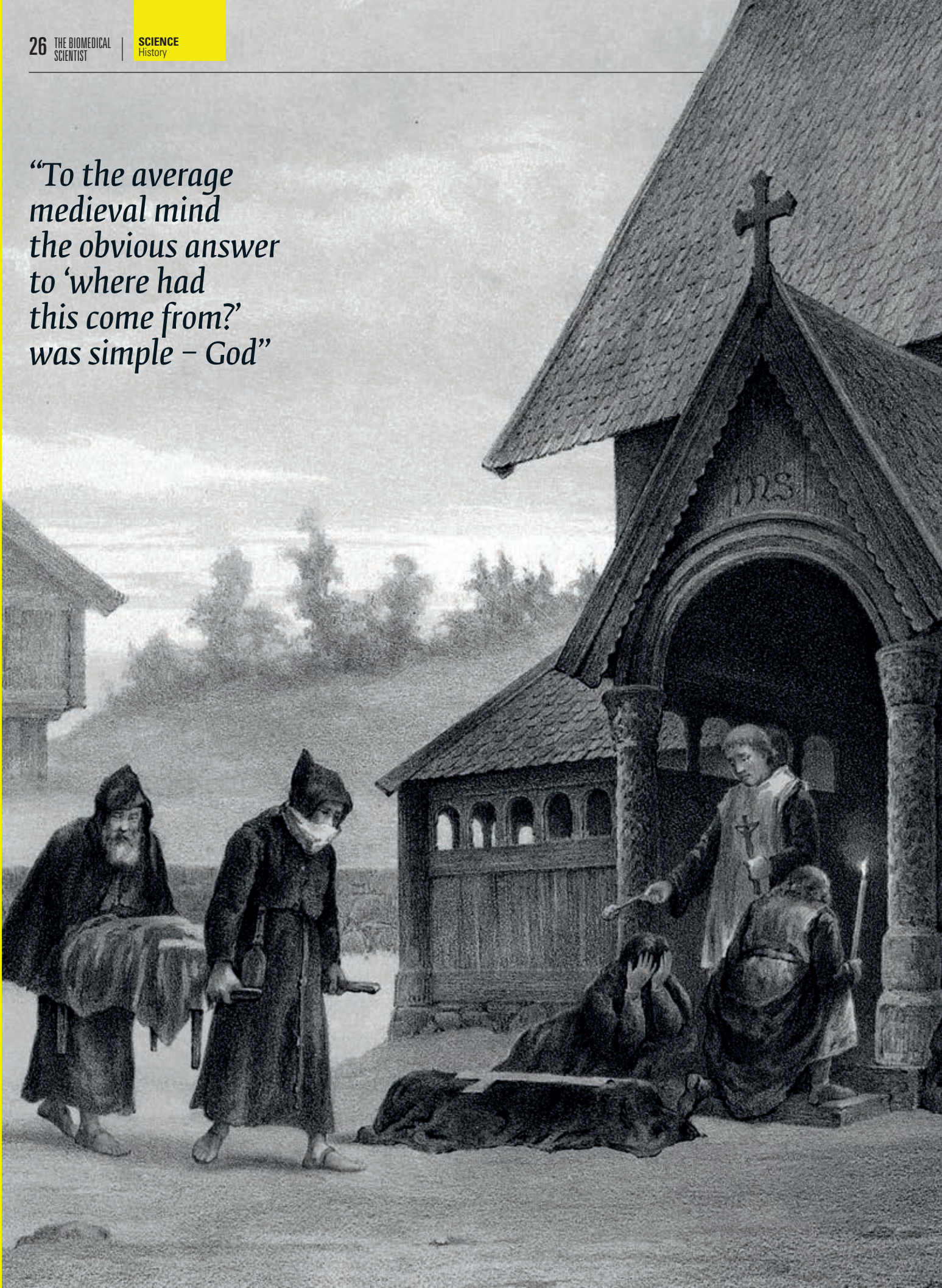
R_0

Ah, the ubiquitous R_o – the basic reproduction number. This is the average number of people each infected person infects. R_o is a function of three factors: (1) the number of contacts an infectious person has; (2) the risk of transmission per contact; and (3) the duration of infectiousness. It is now widely known that while R_o is greater than 1, the epidemic will keep increasing. If we can get R_o down to 1, it will become endemic; that is it will be permanently in the population grumbling along at a low level. However, if we can get R_o below 1, the epidemic will die out. However, R_o assumes that everyone in the population is susceptible, and that there is a complete mixing of the population; that is everyone can come into contact with everyone else. Well, this might be sort of true at the start of an epidemic, but it is certainly not true as the epidemic continues, due to people recovering and becoming immune, improved hygiene practices, and social distancing. Most models are using an R_o for COVID-19 of 2.4. However, have you ever wondered how they actually estimate R_o? Well, they can get an estimate from individual-level contact tracing at the start of an epidemic. However, more commonly it is estimated from population-level data using mathematical models. These models contain parameters like the three factors mentioned above, all of which are usually educated guesses. Unfortunately, this makes R_o an educated guess.

Final thought

I'll leave it at that, but hopefully I have left you with the message that by and large the statistics presented are better than nothing but should be looked at with caution. BMS

"To the average medieval mind the obvious answer to 'where had this come from?' was simple – God"



THE GREAT PESTILENCE

The Black Death was the first great pandemic to devastate these shores and, unlike COVID-19, there was a special horror in the fact no-one knew what it was, states writer **Jonathan Lovett**.

In 1340s England, the Far East seemed a distant, even mythical land. But around 1346, merchants arriving in the ports were telling gruesome tales of whole towns and cities laid to waste by a mysterious illness that had no respect for age or class and which killed its victims in some of the most revolting ways possible.

"It first betrayed itself by the emergence of certain tumours in the groin or the armpits," wrote the Italian author Giovanni Boccaccio at the time, "some of which grew as large as a common apple, others as an egg..."

"As it (the bubo) grew more solid," took up his contemporary, Gabriel de Mussi, "its burning heat caused the patients to fall into a putrid fever... in some cases it gave rise to an intolerable stench. In others it brought on vomiting of blood."

What we now know as bubonic plague began its deadly march along the Silk Road in Asia towards Europe. Not just bubonic, however, but pneumonic and septicaemic plague (all originating from the same source) were heading here in a perfect storm, which was to end up killing between a third and a half of Europe's population.

In one of the first examples of biological warfare it is thought to have entered Europe via a siege of the Crimean city of Kaffa in 1347. The Mongol army, stricken

IMAGE: ALAMY/ISTOCK

by plague, began catapulting infected corpses over the city walls at the Genoese inhabitants. The fleeing traders took the disease back with them to Sicily from where the plague devastated Italy, much of mainland Europe and then, in the summer of 1348, it entered England.

Bad air theory

To the average medieval mind the obvious answer to "where had this come from?" was simple – God. The Bible features many episodes of people sinning and being punished by various forms of plague, ergo unrepentant 14th Century man and woman were being disciplined in the most extreme manner possible. But, while acknowledging that everything proceeds from divine will, the more scientific in medieval society were at a complete loss as to "how is it spread?" and "how on earth can we combat it?"

One of the most authoritative accounts of the time came from the medical faculty in Paris that had looked to the heavens. It reported that a conjunction of three planets – Saturn, Jupiter and Mars – in 1345 had caused a "great pestilence in the air". At the time this chimed with the universal agreement that celestial bodies influenced earthly affairs. So, corrupted air quickly became the predominant theory of how the plague was spread. Certain towns and cities were thought to have a miasma hanging over them, which often resulted in a foul smell, while some even argued that a plague victim might radiate infection in a form of personal miasma, which he or she carried around their head like a halo.

Desperate preventatives

The idea that someone could carry this miasma, or pestilence, around with them was, of course, not too far off the mark. In cities like London, horror stories from Italy had been circulating for months before its arrival with a growing realisation of how easy it was to spread from person to person.

Consequently, there was a run on gloves (much like the recent surge in sales of face masks and antibacterial hand gels) in the capital, as many believed that to touch an infected person was to risk certain death, while surrounding oneself with pleasant smells such as burning juniper was recommended to counter the foul, corrupted air. Monks in Canterbury barricaded themselves into the priory and Gloucester shut its gates to stop entry from outsiders. Everywhere masses and sermons were being held and processions taking place in which the whole community would come out to ask God to forgive them their sins and free them from this dreadful pestilence.

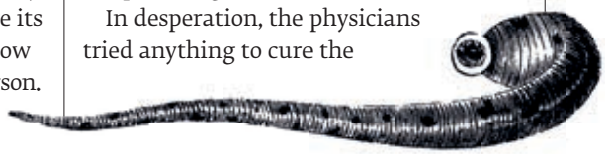
"Living in dirty, squalid conditions, the plague swept through their hovels like fire"

But, without ever suspecting, mass gatherings such as processions would have helped spread the disease and slowly, relentlessly, the plague fanned out from the south coast of England towards the capital of 80,000 inhabitants, arriving in London around the start of November, 1348.

Searching for cures

Outbreaks of disease were a way of life in medieval London, but nothing would have prepared Londoners for the gruesome onslaught that devastated the capital in just over a year. As always, the poor suffered most. Unlike those with money who fled to their country retreats, the poor had to remain and work for their daily bread. Living on top of each other in dirty, squalid conditions, the plague swept through their hovels like fire.

In desperation, the physicians tried anything to cure the seemingly incurable. Bloodletting was still the most popular method – performed on the same side of the body where the buboes appeared. Leeches or emetics were administered in attempts to expel the imbalance of "bad" blood or induce vomiting so the patient could cough out the phlegm and thus restore



balance to the humours. Sweating was also an option. The physician would wrap the poor naked patient in a blanket drenched in cold water, with the idea being the patient would sweat so violently the corruption in their blood would be purged.

How to treat the buboes, or "risings", was more contentious, with some physicians arguing they should be left alone and others contending the boil must be broken and the "foul pestilence" allowed to seep out. To achieve the latter a feather from a pigeon's tail was used or a cup would be heated and placed over the swelling.

Plague sores and swellings were thought to have given off a particular smell, which contaminated the air around the victim so the doctor was recommended to stand near an open window, keeping their nose in something aromatic or hold a sponge soaked in vinegar in their mouth.

However, once the bubo had appeared, little could be done about it. As Boccaccio commented, these swellings were often an "infallible token of approaching death" with the patient invariably suffering three or four days of the agonising pain that accompanied the emergence of the loathsome boil.

Bring out your dead

Although there were instances of people catching the plague and surviving, at least 80% of victims died. In his book *The Black Death in London*, Barney Sloane uses contemporary documents, particularly the rocketing amount of wills drawn up, to suggest the capital suffered a catastrophic mortality rate of 55% or even 60%.

With so much death, the cemeteries were overwhelmed. The Register of Charterhouse recorded: "The violent pestilence killed such a great multitude that the existing cemeteries were insufficient for which reason very many were compelled to bury their dead in places unseemly... For some, it was said, cast corpses into the river."

Facing the prospect of a wave of secondary deaths caused by hundreds of infected corpses lying about, the king, Edward III, acted quickly. He ordered two massive cemeteries to be dug – in West and East Smithfield. Contemporary chronicler Robert of Avesbury tells us he saw 200 bodies being carried to the West Smithfield site nearly every day, which suggests bodies were dumped into the plague pit without due care or respect.

However, an excavation of the East Smithfield plague pit in the 1980s unearthed 759 skeletons (the largest excavation of a Black Death cemetery in the world) and showed the bodies had been deposited with some care – all laid

out neatly in rows. This also suggests some kind of order was still being maintained by the authorities in the face of potential chaos.

Skeletons reveal secrets

In 2014, the Crossrail project unearthed more skeletons from the West Smithfield plague pit close to Barbican. But how could scientists be sure both sets of skeletons were from the Black Death period? Well, carbon dating pinpointed the era, while in the victims' teeth was found the plague bacterium *Yersinia pestis*.

Yersinia pestis infects humans via the Oriental rat flea – *Xenopsylla cheopis*. It causes bubonic, pneumonic and septicaemic plague and different strains of *Yersinia pestis* have been responsible for some of the great disasters in history, including the Black Death, which started what is known as the second pandemic that lasted until the 19th Century.

Several species of rodents are the main carriers of the flea infected with *Yersinia pestis*. However, in the last decade, the popular rat-as-carrier theory has been questioned by some who point out the Black Death rampaged through Europe far faster than modern plague outbreaks obviously spread by rats, while medieval documents have no mention of rats dying in their multitudes. So, the idea that the Black Death was spread by fleas on humans has now been mooted by some academics.

Of course, 14th Century man and woman had no idea about germ theory and it wasn't until 1894 that Alexandre Yersin helped discover *Yersinia pestis* during a plague epidemic in Hong Kong.

Unexpected opportunities

The Black Death petered out in England by the end of 1349, killing around a third of the population. But for those lucky enough to survive its horrors a very different world of possibilities had opened up.

With so many people dying, labour had suddenly become scarce. Your average worker could now charge more for his or

For those lucky enough to survive its horrors a very different world of possibilities had opened up

her work and old agrarian established practices such as serfdom declined as the status and living standards of great swathes of the population improved. It has also been argued that the shortage of labour generated more employment opportunities for women and adolescents.

The blow to another age-old certainty also sparked a greater interest in health and medicine. The high mortality rate of priests and monks shook the absolute authority of the church among ordinary people. While previously the clergy were seen as elevated among the ranks of working-class folk, their very human fallibility in falling victim to the disease, saw a questioning of their role, compounded by the fact many priests had simply abandoned their parishes at the first sign of plague.

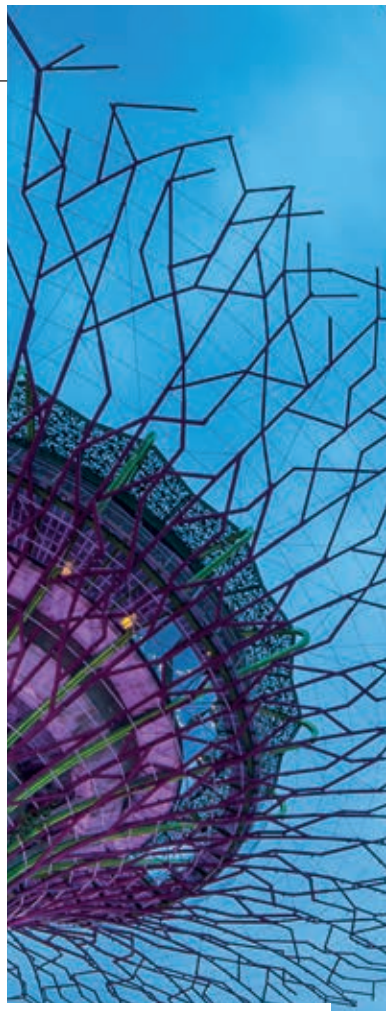
"After 1350 we hear no more of the presage of earthquakes, and little of astrology or even God," notes the historian Samuel Cohn. He writes about a change of mentality after the Black Death, so when plague returned in the 1360s physicians and chroniclers could draw on their knowledge of the previous epidemic and start building a body of work – including a greater understanding of person-to-person infection and the importance of public sanitation – to combat whatever the future held.

In conclusion

Little did they know this future held a further 300 years of pestilence before it finally left England. Following the Black Death, plague returned every 20 years or so until it erupted in a grisly onslaught in 1665. The Great Plague killed at least 100,000 Londoners but was the last time a major plague epidemic broke out in this country. It was followed by the Great Fire of London in 1666, but two miserable years in the capital did lead to something of a renaissance in the arts and the sciences and, ultimately, resulted in a happier, healthier place in which people could live.

At the time, writers referred to the plague as "the Great Pestilence" or "the Great Death" and it was only after the event it became known as the Black Death - the name encapsulating the grim times in which an oft-repeated phrase was "there were hardly enough living to care for the sick and bury the dead".

As we contemplate our own tumultuous time we can at least find some comfort in the fact this epidemic will never approach the terror of what our ancestors had to bear, and bear it they did, with stoicism and without any obvious breakdown in the social order... while we also know exactly what our unseen assailant is and, crucially, how to protect ourselves. BMS



COVID-19: A REPORT FROM MALAYSIA AND SINGAPORE

Professor Anthony Rhodes and **Dr Chooi Ling Lim** discuss the COVID-19 spread and attempts to control the disease in Southeast Asia.

Malaysia and Singapore are located between the Indian Ocean, the South China Sea and the Pacific Ocean. The Malaysian Peninsular is often described as a microcosm of Asia, comprising the three most populous Asian ethnicities and cultures – Chinese, Indian and Malay. Singapore is a highly developed island nation linked to Malaysia by a causeway. It is renowned for its iconic buildings and more recently its super tree groves. It is one of the world's wealthiest nations, with excellent health and public services, and world-leading universities and research and innovation centres.

The outbreak in Singapore

Shortly after the Chinese New Year, on 23 January, Singapore reported its first case of coronavirus in a tourist arriving from Wuhan. Singapore was quick to mobilise health checks and travel restrictions at airports and carry out extensive testing of suspected cases, in addition to contact tracing, with contacts confined to their homes until cleared of infection.

This system worked well until the middle of March, which coincided with the time when globally the seriousness of the disease was beginning to dawn, and when countries started urging their citizens to return. Thousands of Singaporean citizens returned home, with more than 500 carrying the virus. At this time, it was mandatory for returning citizens to stay at home for two weeks. However, other people in the same households were free to carry on their lives as normal. The daily numbers of new cases in Singapore had been low, but by mid-March they increased dramatically, with the majority being linked to imported cases and for the first time not all cases were easily traced. Only recently has it been realised that asymptomatic spread could be a main driver of transmission. Now, all new arrivals in Singapore are sent directly to government quarantine. With the number of people entering the country drastically reducing, so has the number of imported cases.

However, during the first weeks of April the cases in Singapore dramatically increased, coming predominantly from densely packed dormitory accommodation for migrant workers, from countries such as Bangladesh, India, Thailand and Myanmar, working in the construction, shipping and maintenance industries that require a large and low-paid labour force.

The migrants are required by law to live in these vast dormitories, which Singapore has constructed on industrial estates up to 25 kilometres from the city centre. Here men sleep, typically 12 to a room, in bunks, with shared bathroom, cooking and social facilities. The dormitories are clean and have all essential and recreational facilities and, whilst this segregation of migrant workers from the rest of the population is controversial, the conditions are probably better than the migrants would have found in privatively run boarding houses. In such densely packed accommodation, social

distancing is impossible. These dormitories resulted in new clusters of COVID-19 in early April, with nearly 500 new cases arising from just one facility. The fear is that these numbers will dramatically increase in the coming weeks. More than 24,000 workers have now been confined to the dormitories after Singapore's partial lockdown in early April.

The outbreak in Malaysia

Malaysia traces its first cases of COVID-19 to 25 January, when travellers from China arrived via Singapore. The number of reported cases was low at this time, then clusters began to appear in March, linked to the Tabligh Jama'at religious gathering, held in Kuala Lumpur and attended by 16,000 people, including 1500 foreigners.

Subsequently, the gathering emerged as a source of hundreds of new infections, spanning Southeast Asia, and to date accounts for 40% of all Malaysian COVID-19 cases. Within a few weeks Malaysia had the largest number of COVID-19 cases in the region, with over 2000 infected cases by the end of March, compared with only 30 at the beginning of the month.

In an attempt to control the spread of the disease, Malaysia began to shut its borders, restrict movement and close all but essential services. Since then, Malaysia has seen regional outbreaks of COVID-19, frequently in places where people are living in old and crowded conditions. One of the latest outbreaks is in apartment blocks in downtown Kuala Lumpur. At the time of writing, some 6000 residents in these buildings are completely locked down in an enhanced movement control order (EMCO), after 15 residents were found to have the disease. The buildings are surrounded with barbed wire barricades, a heavy police presence and officials in white protective clothing move in and out. These densely packed old apartment buildings are home to mostly poor migrant workers. This is the fourth EMCO ordered by the government, which collectively involve 16,700 people.

TABLE 1. POPULATIONS AND DEMOGRAPHICS FOR MALAYSIA, SINGAPORE AND THE UK (AS OF APRIL 14)

	Malaysia	Singapore	UK
Population	32.4 million	5.9 million	67.9 million
Median age (years)	30.3	42.2	40.5
Climate	Tropical	Tropical	Temperate
Average annual temperature	28-32°C	25-31°C	6-14°C
Date of 1st COVID-19 case	25 Jan 2020	23 Jan 2020	31 Jan 2020
Date of MCO	18 Mar 2020	7 Apr 2020	23 Mar 2020
Total COVID-19 cases	4987	2918	89,571
Total deaths	82	9	11,347

Impact on health services

In Malaysia the epicenter of the COVID-19 infections has been Kuala Lumpur. Two of the main government hospitals coping with the COVID-19 cases are Hospital Kuala Lumpur and Sungai Buloh Hospital. Historically, the latter was a leprosy centre for the region and was recently designated the main COVID-19 referral centre for the area. Many of the staff have been working 12-hour shifts for up to 12 days to cope with the influx of COVID-19 patients. The Malaysian Institute of Economic Research has predicted cases will peak at around 8000 to 9000. Consequently, university hospitals in Kuala Lumpur and its environs have also started to cater for increasing numbers of COVID-19 patients. This has inevitably led to the cancellation of elective surgery and many clinics. But in contrast to many countries where the health services are being severely stretched in the response to COVID-19, Singapore's hospitals appear to have adequate capacity and facilities.

COVID-19 testing

The Malaysian Institute of Medical Research was initially the only testing laboratory for COVID-19 in Malaysia. However, by early April, the number of approved centres increased to 43. While the RT-PCR test has predominated, the health authorities both in Singapore and Malaysia are looking to bring in more rapid antigen testing with the hope of increasing the number of tests from around 11,500 per day to 16,500 per day. The Malaysian Ministry of Health is also negotiating the purchase of additional PCR machines from China to increase the capacity of RT-PCR testing.

In order to address the urgent need for COVID-19 testing in Singapore, its Health Sciences Authority (HSA) has been provisionally approving a range of COVID-19 testing kits. Those tests receiving provisional authorisation from HSA are then allowed to be supplied to healthcare institutions in Singapore. Singapore is a renowned regional science and innovation

hub, and this is reflected in some of the products being produced locally in response to the COVID-19 outbreak.

Movement, food and toilet rolls

The movement control order (MCO) in Malaysia came into force on 18 March and was extended to the end of April. According to the Oxford COVID-19 Government Response Tracker, it is the fourth most restrictive in Southeast Asia. The University of Oxford tracker produces a score based on seven response indicators. While less strict than that of Laos, Vietnam and the Philippines, Malaysia's MCO is stricter than that imposed in the UK and the US. However, a higher score does not necessarily mean more efficient control of COVID-19, just restrictions that are more stringent. The MCO in Malaysia has suspended all but essential businesses. The campuses of all universities and schools are closed and were instructed to suspend all teaching for two weeks from 18 March, then revert to online e-learning until the MCO is lifted.

Travel is banned domestically and internationally, with flights to neighbouring countries cancelled. Over 700 roadblocks have been put in place on many of the highways and in towns and residents not providing essential services are only permitted to leave home to buy food. Exercising and sports outside the home are banned. Failure to comply with the MCO results in a fine of RM1000 (around £200). So far, over 7000 people have been arrested, including youngsters playing football and people out jogging. Perhaps a bigger deterrent than the fine is the prospect of being handcuffed and detained in the local police station whilst awaiting the charge. Some Malaysians have expressed their opinion that while perhaps the fine should be increased, the transgressors should not be treated like hardened criminals or terrorists, as many are first-time offenders. A local newspaper recently released the results of a poll emphasising that nearly half of all Malaysians surveyed supported the MCO extension. However, if you choose to interpret the results the other way the poll also shows that the majority (slightly greater than half) did not support it.

Singapore in early April passed a new law that is effectively a partial national lockdown, although this term is not used, prohibiting everyone from leaving their homes except for essential activities (which does include exercise). The penalty for transgressing this law is a fine of S$10,000 (£5600) or six months in prison. Within the first two days of the new law, over 10,000 warnings were issued. However, Singaporeans are renowned for trusting the ruling government and are very likely to abide by the law once they have fully understood its implications.

Unlike the UK where, at the time of writing, queues outside supermarkets appear to be a daily occurrence, this has not occurred in Malaysia, except on the eve of the MCO, when there was panic buying. However, within a few days the shops had re-stocked their shelves with essentials, and this remains the case some weeks after the MCO commenced.

"Residents not providing essential services are only permitted to leave home to buy food"

IMAGES: SHUTTERSTOCK

On a more lighthearted note, unlike some countries, supply of toilet rolls in the supermarkets has not been an issue. This is less of a necessity in Asia, as the vast majority of private and public toilets have a bidet system, arguably a much more sensible device than a roll of Andrex.

Concluding remarks

The common denominator for the subsequent waves of the epidemic in Malaysia and Singapore is densely crowded living conditions, frequently the homes of migrant workers from the region's poorest countries. Perhaps there is a message here for all of us to address some of the social inequalities of the world, not just because it is the right thing to do, but because the COVID-19 virus does not discriminate or respect borders or postcodes. It can bring down the Oxford-educated Prime Minister of the UK living in 10 Downing Street, just as it can the uneducated and impoverished child living in the slum districts of Jakarta. If densely packed and crowded housing conditions are a breeding ground for the continued spread of COVID-19, then in order to control the disease, we all have a vested interest in providing better living conditions for the poorest members of society, so that social distancing and basic hygiene can actually become a reality. The Malaysian Prime Minister, Tan Sri Muhyiddin Yassin, in his address to the nation on the evening of 10 April, said: "We cannot go back to the way we were before." This is very true for all of us, no matter where we live. However, exactly what the new "norm" will be remains to be seen. BMS

Anthony Rhodes is a Professor and **Dr Chooi Ling Lim** is a Senior Lecturer in the Division of Applied Biomedical Sciences & Biotechnology at the School of Health Sciences, International Medical University, Kuala Lumpur, Malaysia

MORPHOLOGY: IS THE FUTURE DIGITAL?

Biomedical Scientist Team Manager **Tahmina Hussain** puts a new automated digital analyser to the test.

Full blood count samples requiring morphological examinations are one of the most valuable investigations in the haematology laboratory, due to their significant contribution towards the diagnosis and monitoring of disease processes. It is imperative that these procedures can be completed as quickly as possible, especially in cases where immediate clinical action is required.

Manual light microscopy is considered the gold standard for reporting morphology of blood cells. This method is time consuming at The Christie NHS Foundation Trust, where the main diagnoses in the haematology laboratory consist of haematological malignancies, and the presence of abnormal white blood cells contributes towards the heavy workload. Limitations include subjective interpretation of cells and variation in results reported between individuals. Due to the nature of the malignancies being monitored post-chemotherapy, many samples are leucopenic, which carries a further challenge of counting and identifying the adequate number of cells required in order to provide an accurate manual differential. Development of automated digital morphology analysers has made it possible to identify white blood cells, which improves turnaround times and reduces subjectivity in the interpretation of cells.

Digital morphology

Performing manual differentials is highly demanding on time, as well as requiring experienced staff and this has an effect on turnaround times, particularly during night shifts and weekends, when the availability of trained staff may be limited. The introduction of a digital morphology analyser may be a solution to overcoming these challenges. Additional benefits of introducing a digital morphology analyser in the haematology laboratory include speeding up the process for training on morphology, as the database stores images of the cells examined in the peripheral blood smears in a reference library that is accessible to trainees. The communication between staff and consultants can be improved as the blood smears can be reviewed through email or by logging into the software system remotely.

At the Christie Trust, full blood count samples are processed using optical scatter methods and cytochemistry. The results are presented on cytograms where the populations of cells are displayed in

distinct clusters. Abnormal flags will indicate that the differential may not be correct and this alerts the operator to delete the differential and refer the sample for a peripheral blood smear to be examined.

The digital morphology analyser identifies white blood cells and classifies them into the different categories of immature granulocytes and a digital image is captured by the camera. These are then presented to the operator for verification or reclassification of the cells. The tools for the preclassification of these cells into their categories have been developed over the past few years using neural networks and quantitative measurements, which are divided into geometric, colour and texture characteristics. These include obtaining information on the morphological features based on the pattern, shape and size of cells, nuclear-cytoplasmic ratio, colour intensity and nuclear density of cells.

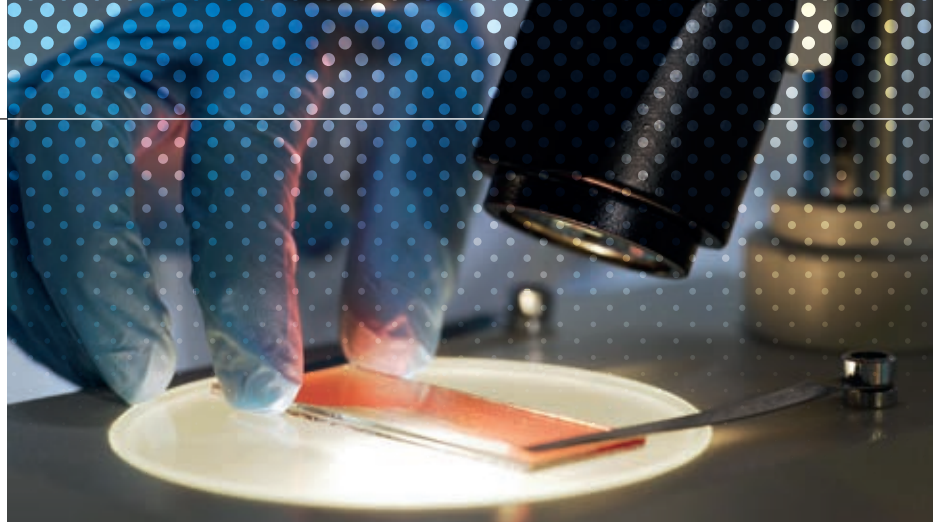
A study was carried out to investigate whether turnaround times for reporting manual differentials on peripheral blood smears can be improved and whether there was a difference in results obtained using manual microscopy compared with an automated digital morphology analyser.

Materials and method

Full blood count samples from the routine workload were processed on the standard analysers. Samples that fell into a "normal" category with no abnormalities were included in the investigation as controls. Further samples were selected that were referred for a manual differential due to abnormalities flagged by the analyser. The abnormal flags in the inclusion criteria consisted of large unstained cells over 0.5 x 10^9/L, the presence of myeloperoxidase deficiency, atypical lymphocytes flags, immature granulocytes and blasts flags with a white blood cell count of over 1.0 x 10^9/L. A peripheral blood smear was prepared for each slide and a 100-cell manual differential was performed by two biomedical scientists.

The final result was reported as the average of the manual differential counts obtained for each cell type and the average of the time taken to perform the manual differentials was also calculated for the abnormal slides. The same smears were then processed on the automated digital analyser. Each cell type that was classified by the system was then either approved or reclassified to another cell type by the biomedical scientists. The time

IMAGES: ISTOCK



taken was recorded to compare with the time taken to perform the manual differentials. Statistical analysis was performed using correlation coefficient values to establish the relationship between the values obtained for each white blood cell type using both methods of microscopy. Bland-Altman plots were used to investigate the agreement between the two methods and Passing-Bablok regression analysis was performed to determine any systematic or proportional differences between methods.

Results

Results of the study indicate that although a higher correlation between the reference and test method was found for the more mature white blood cells, there were significantly weaker correlations between both methods for the immature granulocyte counts. It is imperative to note that the incorrect classification of the immature granulocyte cell types by any one of the methods would only have a clinically significant outcome if they were substantially different. The more immature the cells are, the more severe the case requiring a more intensive treatment plan. This would make a clinically significant difference for the diagnosis of acute promyelocytic leukaemia, where the higher the number of promyelocytes present, the more likely the patient is at risk of haemorrhagic death.

Limitations

On reviewing the results of the peripheral blood smears on the digital morphology analyser, there were certain cell types that were preclassified as incorrect cell types and required reclassification prior to validation of the results. Basophils have distinct properties, such as dark cytoplasmic granules, which may also be seen in neutrophils in the peripheral blood smears from patients with infection or inflammatory conditions, such as sepsis. However, the neutrophils with toxic granulation were incorrectly preclassified as basophils.

The reference library is used only as a visual aid for the operator as the preclassification criteria on the system is fixed via an internal algorithm; the criteria for the preclassification cannot be altered on the system, therefore, the operator can only reclassify the cells that have been incorrectly classified. It would be useful to be able to adjust the settings to allow the system to preclassify the cells referring to the modified reference library as this will allow a more individualised preclassification of cells according to the types of cells seen in different laboratories.

Conclusion

This study demonstrated that the digital automated analyser did not reduce the time taken to perform manual differentials and that the immature white blood cells had a lower percentage of preclassifying agreement. However, The Christie Trust is a hospital that specialises in cancer and the diseases that are commonly diagnosed in the haematology laboratory with the use of flow cytometry, peripheral blood and bone marrow smears are haematological malignancies. So the use of automated digital morphology analysers alone may not be appropriate for completing manual differentials here.

However, with modifications to the pre-fixed algorithms, there is the potential to revisit the possibility of introducing such a system. It would be beneficial in a general hospital where immature granulocytes as a result of malignancies and chemotherapy are less commonly encountered.

Future experimentation

Additional work is required for the development and improvement in the skills of the digital, automated system when classifying immature white blood cells. This would involve modification in the fixed algorithms. The next stage of the development in morphology will be to introduce an automated digital morphology system within a full blood count analyser that will process the full blood count, prepare and examine the peripheral blood smear and provide results that will be sent directly to the laboratory information system without any physical involvement. More emphasis on the investigation of red blood cells is required, as more attention is focused on the evaluation of abnormal white blood cells. The digital automated system is very useful in the identification and grading of red blood cell abnormalities.

Although further work is required for the development of the preclassification of immature white blood cells, overall, the digital automated system has many benefits, including reduced eye strain, the ability to review the results and use results for training. It is important to note that the new system does not replace an experienced biomedical scientist in morphology, but can replace the microscope in many instances; however, morphology skills are still required. The analyser is an excellent system that can be used as a tool for teaching, quality assurance and also for completing staff competency assessments. BMS

Tahmina Hussain is a Biomedical Scientist Team Manager and Blood Sciences Training Officer at the Christie Pathology Partnership. She would like to thank her supervisor **Dr Nina Dempsey-Hibbert**, for supervision and guidance.

FUJIFILM
Value from Innovation

The New Generation Dry Chemistry Analyser

Connecting to the **future**
A new world of dry chemistry

190 tests per hour
28 colorimetry tests
3 electrolyte tests

Automated Clinical Chemistry Analyzer **NEW**

DRI-CHEM NX700

A Complete NPT Solution
- Combining Dry Chemistry and Haematology

NEW
DRI-CHEM IMMUNO AG2

Boule

DRI-CHEM NX10N

Fecal Occult Blood Analyzer
QUICK RUN (II)

FUJI DRI-CHEM
NX500
Automated Clinical Chemistry Analyzer

medicalsales_uk@fujifilm.com • www.fujifilmivd.com • 01234 326780

IBMS COVID-19 RESOURCES

The IBMS has created an area in the resources section of its website that houses all materials and information relating to **COVID-19**. It includes guidance, formal statements and discipline-specific content.

Guidance

Guidance from organisations including the UK Government, Public Health England, the Royal College of Pathologists and UKAS, among others. This page contains dozens of links to the latest guidance. Content ranges from standard operating procedures for COVID-19 testing in NHS laboratories, to guidance on care of the deceased.

News and general information

The latest relevant news and general information for laboratory staff in relation to COVID-19. Sources for the information include the IBMS, NHS Digital, the Health and Care Professions Council and *The British Medical Journal*.

Statements and responses

Official statements, responses, comments and letters from professional bodies and organisations. This includes government bodies, the Science Council and the IBMS. Content ranges from an IBMS letter that can be given to schools and nurseries to explain that biomedical scientists are key workers, to a statement from UK Chief Allied Health Professions Officers and the Health and Care Professions Council regarding returnees to the Register to respond to coronavirus demand.

Research articles and documents

Relevant research articles and documents that may be useful for laboratory staff members. Publications featured include *Nature, The Lancet, JAMA* and *the American Journal of Haematology*, among others.

This page contains dozens of links to the latest guidance, from laboratory SOPs, to info about care of the deceased

Haematology

This is one of the smaller areas of the website and contains a link to the British Society of Haematology's COVID-19 updates.

Health and wellness

A variety of sources dedicated to maintaining health and wellbeing during the pandemic. The page is broken up into the following topics: exercise, sleep-well tips, coping with self-isolation/social distancing, money-saving tips, music and mentoring opportunities. Resources range from links to free online opera and ballet performances to guidance on maintaining good mental health.

In the press

Link to all mentions of the IBMS in the news coverage.

For parents

For all IBMS members with children, this page includes a variety of resources to help stay active and motivated. Content ranges from a Q&A on COVID-19 and pregnancy, childbirth and breastfeeding, to home-schooling sessions from celebrities including Professor Brian Cox (science), Carol Vorderman (maths) and David Walliams (English). IBMS

All these pages are updated as soon as new information becomes available. Any members who wish to suggest content, or who have resources they would like to share, are asked to contact the communications team at **communications@ibms.org**

MY IBMS NEWS

LOBBYING

AVOID "WILD WEST TESTING"

The IBMS has circulated a statement to all major media outlets and MPs stating that we must avoid a "Wild West testing" scenario in the UK.

The statement from IBMS President Allan Wilson stresses that members are "increasingly expressing their frustration" that it is a global supply shortage holding NHS biomedical scientists back, not a lack of capacity.

He continues: "The profession is now rightly concerned that introducing these mass testing centres may only serve to increase competition for what are already scarce supplies and that NHS testing numbers will fall if their laboratories are competing with the testing centres for COVID-19 testing kits and reagents in a 'Wild West testing' scenario. The UK must avoid this for the sake of patient safety."

The statement goes on to stress the vital importance of HCPC registration and UKAS laboratory accreditation to protect patients and the public.

Allan also thanks the biomedical scientists and lab staff "who are going above and beyond to help the nation".

IBMS NOTICE

ANNUAL GENERAL MEETING

In light of current travel restrictions and Government guidance on COVID-19, the IBMS is reviewing the arrangements for its Annual General Meeting and will confirm the details as soon as able.

COVID-19 UPDATES

For all the latest news, announcements and COVID-19 updates from the IBMS and the biomedical science profession, visit **ibms.org/resources/news**.

Any members who wish to contribute a news story are asked to email details to **news@ibms.org**. As well as posting on the website news section, the IBMS also uses social media channels to promote and reach a larger audience.

IBMS QUALIFICATIONS

Changes to IBMS exams

Due to the pressures and difficulties caused by the COVID-19 there are changes to some IBMS exams in 2020.

These changes apply to the Diploma of Expert Practice (DEP) in Histological Dissection and Immunocytochemistry, the Higher Specialist Diploma (HSD) and the Advanced Specialist Diploma (ASD) in Specimen Dissection.

The closing date for applications to sit these examinations in 2020 has been changed from 1 May to 26 June.

The portfolio submission deadline has been changed from 22 May to 31 July.

DEP and ASD exams were scheduled to take place on 7 September at the University of Westminster, Glasgow Caledonian University and the Jordanstown Campus of Ulster University.

At the time of publication, it had not been decided whether the exams will go ahead on this date or be moved to later in the year.

The HSD exams will not take place as planned on 7-8 September. A new date and the locations for the exams have yet to be set, but it is hoped to be in November or early December.

→ **For information on all other IBMS qualifications and updates on the above, keep checking the appropriate pages of the IBMS website, or email examinations@ibms.org**

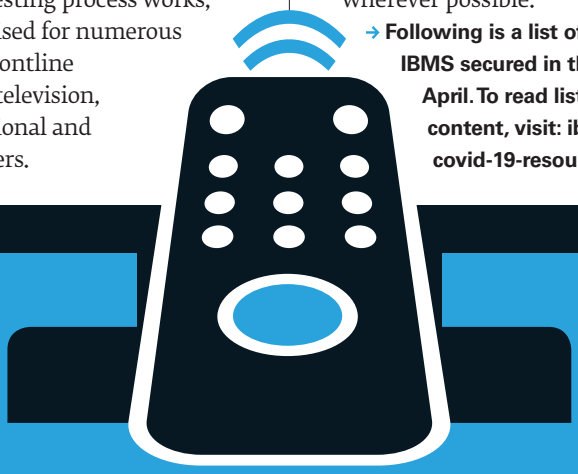
IBMS IN THE MEDIA

Since COVID-19 first arrived on these shores, the IBMS has been working hard to communicate the vital work that biomedical scientists are doing to help tackle the pandemic and protect the public.

Whether this is through raising awareness of what the profession contributes, or by debunking myths about how the testing process works, the Institute has organised for numerous members of staff and frontline scientists to appear on television, on the radio and in national and international newspapers.

All this coverage can be accessed though the IBMS website, with links to the relevant media wherever possible.

→ **Following is a list of media appearance the IBMS secured in the first two weeks of April. To read listen to and watch this content, visit: ibms.org/resources/covid-19-resources/in-the-press**



National television

Interview between IBMS President Allan Wilson and Victoria Derbyshire
BBC One and BBC News,
15 April 2020, 9.15am

Interview with IBMS President Allan Wilson and Kay Burley
Sky News, 7 April 2020

National radio

Interview of IBMS President Allan Wilson
BBC Radio Scotland, 15 April 2020
LBC Radio, 9 April 2020

BBC Radio 4, 5 and 6 news bulletins
4 April 2020

BBC Radio 5 Live Stephen Nolan show
3 April 2020

National and international newspapers

UK expected to miss 100,000 a day virus testing target
Financial Times, 15 April 2020

Here's How The UK Plans To Go From 16,000 Tests A Day To 100,000 By The End Of The Month
Buzzfeed, 10 April 2020

NHS staff forbidden from speaking out publicly about coronavirus
The Guardian, 9 April 2020

Pandemic shows us why a strong science community is essential – Rebecca Wright
The Scotsman, 7 April 2020

Government plan to roll out antibody testing attacked
Financial Times, 6 April 2020

Government's 100,000-a-day coronavirus testing pledge 'not achievable', fear scientists
Mirror Online, 5 April 2020

Matt Hancock looks emotional as he reveals he's lost 'two people he was fond of' from the coronavirus outbreak during national press conference
Daily Mail, 5 April 2020

NHS officials 'screaming' at factory chiefs for more tests: Manufacturers say they have been 'completely overwhelmed' by demand and cannot 'magic ten million kits out of thin air'
Daily Mail, 5 April 2020

100,000 Tests A Day 'Is Impossible': NHS Scientists Warn Matt Hancock's Plan Is In Serious Doubt
Reporter.AM, 4 April 2020

100,000 tests a day 'is impossible': NHS scientists warn Matt Hancock's plan is in serious doubt
Daily Mail, 4 April 2020

UK coronavirus testing: Matt Hancock confirms 100,000 test target won't include antibody tests
inews, 3 April 2020

Health specialists 'frustrated' at lack of resources to ramp up Covid-19 testing
Express and Star, 3 April 2020

Scientists ask for more detail on UK's coronavirus testing target
Financial Times, 3 April 2020

Why has the UK lagged behind in testing for the coronavirus?
The Guardian, 3 April 2020

UK opens first COVID hospital but criticism of testing plans mount
Euractiv.com, 3 April 2020

UK ministers struggle to keep promise of 100k coronavirus tests by end of April
The Guardian,
3 April 2020

IMAGES: ISTOCK/SHUTTERSTOCK/GETTY

JOURNAL-BASED LEARNING EXERCISES

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

DEADLINE WEDNESDAY 5 AUGUST 2020

Primaquine-induced haemolysis in females heterozygous for G6PD deficiency. Chu CS, Bancone G, Nosten F, White NJ, Luzzatto L. *Malar J* 2018; **17** (1): 101. doi: 10.1186/s12936-018-2248-y. Assessment No: 050420

01	G6PD deficiency is an autosomal rather than X-linked condition.	11	Females with an intermediate phenotype will definitely be heterozygotes.
02	Erythrocytic G6PD activity decreases physiologically as erythrocytes age in the circulation.	12	Doxiadis *et al.* observed that newborns with low levels of G6PD in their red blood cells had an increased frequency of neonatal jaundice, which was often severe.
03	In most malaria-endemic areas, testing for G6PD deficiency is available.	13	Over the past 90 years, 8-aminoquinolines have been prescribed mostly with testing for G6PD deficiency.
04	Primaquine was the first 8-aminoquinoline used for the radical curative treatment of *Plasmodium vivax* malaria.	14	In females, if the G6PD activity is ≤25% of normal, females receive the same treatment as G6PD-deficient males.
05	Nitrofurantoin, ciprofloxacin and rasburicase are known to cause haemolysis in G6PD-deficient individuals.	15	Tafenoquine has a long terminal elimination half-life which allows a single dose to be given. Thus, unlike primaquine, which can be stopped at the first sign of toxicity, tafenoquine cannot be stopped.
06	The extent of haemolysis in patients receiving tafenoquine was greatest following the administration of 200-mg doses of this drug.	16	In somatic cell mosaicism, the ratio of the two cell types that make up the mosaic is the same for all females.
07	Anecdotal evidence of G6PD deficiency has been recorded since antiquity.	17	Lyonization refers to the random inactivation of one X-chromosome in the somatic cells of a female.
08	The average proportion of G6PD-deficient red cells in heterozygotes is 50% and will always be less severe than a hemizygous male.	18	In a male population there are two evident phenotypes; G6PD normal and deficient.
09	In normal subjects, G6PD activity is often around 7–10 IU/gHb.	19	The WHO malaria treatment guidelines have long recommended the addition of primaquine to chloroquine (or now to artemisinin-based combination therapy) for the treatment of *P. vivax* and *P. ovale*, and this recommendation is often followed.
10	Males with a G6PD-deficient phenotype are hemizygous for a mutant allele.	20	As malaria programmes progress towards the elimination of *P. falciparum* malaria, the proportion of malaria infections attributable to *P. vivax* outside sub-Saharan Africa declines.

REFLECTIVE LEARNING

01	Critically discuss the challenges a laboratory would face when introducing testing for red cell enzymopathies.	02	Red cell polymorphisms provide a selective advantage in areas of high malaria prevalence. Critically discuss this statement.

DEADLINE WEDNESDAY 5 AUGUST 2020

An audit of liquid-based cytology samples reported as high-risk human papillomavirus and borderline nuclear change in endocervical cells. Manley KM, Luker R, Park C. *Cytopathology* 2020; **31** (2): 130–5. https://doi.org/10.1111/cyt.12803. Assessment No: 050820

01	This audit was a prospective study carried out between 2016 and 2018.	11	The sensitivity, specificity, PPV and NPV were calculated on the colposcopic assessments of high-grade dysplasia for the women in the audit.
02	68.2% of the patients identified for this study had high-grade dysplasia at diagnostic biopsy.	12	The age range of women identified in the audit was 25–49 and the majority of these were smokers (81.8%).
03	The positive predictive value (PPV) of colposcopic impression was 100% and the negative predicative value (NPV) was 43.8%.	13	Eight of the 22 women in the audit were found to have CIN2 or CIN3, and seven were found to have CGIN.
04	The incidence of borderline change in endocervical cells in this study was 1.2%, which falls into the range identified in the referenced literature of 0.5–1.8%.	14	The time from referral to attendance at colposcopy for the 15 women with high-grade dysplasia varied from two to 12 weeks with a median of four weeks.
05	NHSCSP guidance released in 2016 recommended all women with BNC in endocervical cells and high-risk HPV (HR-HPV)-positive on triage should be seen in colposcopy within two weeks of referral.	15	There was a difference in patient characteristics between the women identified with low-grade versus high-grade dysplasia.
06	NHSCSP guidance issued in 2016 for the management of women with BNC in endocervical cells and HR-HPV-positive was based on evidence prior to the introduction of HPV triage.	16	One patient in the audit had a type 3TZ on colposcopic impression, with the remaining 21 patients having either a type 1 or type 2TZ.
07	Evidence used in the NHSCSP guidance from 2016 indicated rates of 10–33%, 10% and 1.8–22% for CIN, CGIN and invasive lesions, respectively, in women with BNC in endocervical cells.	17	Colposcopic assessment was found to have a specificity of 100% and sensitivity of 37.7% for high-grade dysplasia in women with aTZ type 1–2.
08	Evidence from outcomes following HPV triage suggest 50–62% of women with BNC in endocervical cells and HR-HPV-positive will have high-grade changes requiring treatment.	18	The authors suggest the audit findings support the USA recommendations of endocervical sampling for all women with any grade of glandular changes reported on cytology, irrespective of colposcopic impression.
09	Guidance issued by the British Association for Cytopathology (BAC) in 2014 suggested MDT discussion for women with a cytological glandular abnormality, either BNC or ?neoplasia, confirmed on histopathology or colposcopy should be reviewed at MDT.	19	23% of the women did not attend colposcopy within the NHSCSP-recommended timescale of six weeks from referral date, and, of these, three had CIN3 and two had high-grade CGIN at LLETZ.
10	The data collected and recorded were identifiable to each individual patient.	20	If all cases of BNC in endocervical cells are treated as high-grade referrals (seen in two weeks) as the authors recommend, this will likely have a significant impact on the workload of colposcopy departments.

REFLECTIVE LEARNING

01	Carry out an audit of the cases between 2016 and 2018 reported within your laboratory as BNC in endocervical cells, and the outcomes. Do your findings correlate with the findings identified in this study?	02	Did the management in these cases adhere to NHSCSP guidance at the time? Could the authors' suggested algorithm here have resulted in a more favourable outcome for the patients identified in your audit?

EVENTS AND TRAINING COURSES

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

DATE	TITLE	VENUE CONTACT
September		
2 Sep	**UK NEQAS Cellular Pathology Technique Introduction to Immunocytochemistry Workshop**	Northumbria I cpt@ukneqas.org.uk
2 Sep	**UK Standards for Microbiology Investigations: Steering Committee Working Group Meeting September 2020**	London I Public Health England
3 Sep	**UK NEQAS Cellular Pathology Technique Advanced ICC Applications in Laboratory Practice B Workshop**	Northumbria I cpt@ukneqas.org.uk
7-25 Sep	**HPLC Masterclass Course**	Rochester I stuart@laserchrom.com
14-18 Sep	**Flow Cytometry Course**	York I katejermey@rms.org.uk
17 Sep	**EntericBio Molecular GI Conference**	Limerick, Ireland I sflanagan@serosep.com
October		
5-6 Oct	**Introduction to Practical HPLC Course**	Rochester I stuart@laserchrom.com
7-8 Oct	**Agilent HPLC Equipment Servicing Course**	Rochester I stuart@laserchrom.com
7-8 Oct	**Intermediate Practical HPLC Course**	Rochester I stuart@laserchrom.com
12-14 Oct	**Practical HPLC Method Development Course**	Rochester I stuart@laserchrom.com
14 Oct	**UK NEQAS Cellular Pathology Technique Mohs workshop**	Gateshead I cpt@ukneqas.org.uk
15 Oct	**UK NEQAS Cellular Pathology Technique Renal workshop**	Gateshead I cpt@ukneqas.org.uk
November		
1 Nov	**Scottish Pathology Network Annual Event**	Edinburgh I NSS.SPAN@nhs.net
4 Nov	**UK Standards for Microbiology Investigations – Chairs Strategy Working Group Meeting**	London I Public Health England
9-13 Nov	**Advanced Practical HPLC Course**	Rochester I stuart@laserchrom.com
11 Nov	**UK NEQAS Cellular Pathology Technique Non Gyn Cytology Beginners/ Refresher Workshop**	Gateshead I cpt@ukneqas.org.uk
12 Nov	**UK NEQAS Cellular Pathology Technique Non Gyn Cytology Intermediate Workshop**	Gateshead I cpt@ukneqas.org.uk
16 Nov	**UK NEQAS Cellular Pathology Technique BMT workshop**	Gateshead I cpt@ukneqas.org.uk
25 Nov	**UK NEQAS Cellular Pathology Technique TEM workshop**	Leicester I cpt@ukneqas.org.uk
27 Nov	**Ortho Clinical Diagnostics Transfusion Medicine User Group Meeting**	East Midlands I Hayley.thomson@orthoclinicaldiagnostics.com
December		
14-15 Dec	**Advanced Agilent HPLC Equipment Servicing Course**	Rochester I stuart@laserchrom.com
2 Dec	**UK Standards for Microbiology Investigations Joint Bacteriology and Virology Working Group Meeting**	London I Public Health England

Azlon® Round Integral Wash Bottle

Azlon®

REUSABLE PLASTIC LABWARE

- Designed for increased protection against contamination
- Unique vented cap with a PTFE membrane to eliminate hazardous solvent drips
- Available plain or pre-printed with chemical names and information compliant with European safety legislation

Solutions to suit your liquid handling needs

SciLabware

SciLabware is a company of **DWK Life Sciences**

For more information visit **www.scilabware.com**

Email us with your questions **enquiries@scilabware.com**

SciLabware Limited, Unit 4, Riverside 2, Campbell Road, Stoke-on-Trent, ST4 4RJ, UK

Tel: **+44 (0)1782 444406** | Fax: **+44 (0)1782 940436**

HERE TO HELP

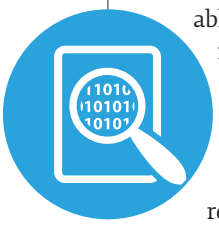
VIRTUAL VERIFICATION

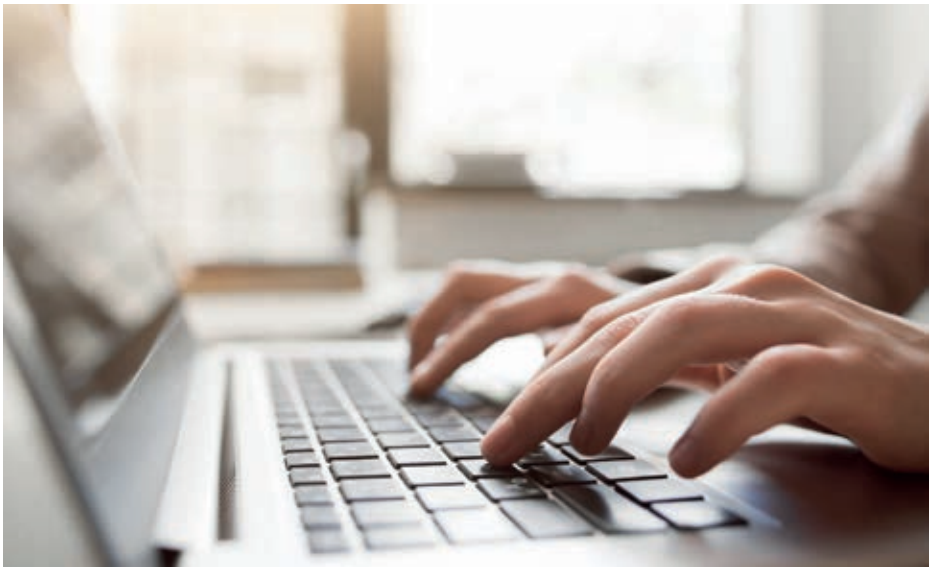
IBMS Deputy Head of Education **Jocelyn Pryce** explains the new verification process and the impact that it had in just a few weeks.

The coronavirus pandemic has seen major changes in all our lives. We had, for some time, been considering the suitability of the verification and examination processes. Then the situation that began to emerge a few months ago challenged us to look for alternatives.

While historically the laboratory visits were an integral part of the assessment process, we have been struggling to find volunteers to keep abreast of the numbers of assessments required. Our pools of verifiers and examiners have been finding it increasingly difficult to find time away from the laboratory to undertake the assessments and despite their willingness to help others progress in the profession, they have had to refrain from stepping up and volunteering.

The result of this was two-fold; slower turnaround time in identifying verifiers or examiners to undertake assessments and those who were still able to undertake them being overloaded with requests. In the middle of March, and in response to the Government advice regarding travel, we informally suggested that trainers considered virtual assessments and early feedback was very positive. So, a week later we rolled out our new process of virtual verifications. The changes to the process itself are minimal. At the end of March we put a call out for verifiers to help us to put as many trainee biomedical scientists on the HCPC register as possible by undertaking verifications.





The move to virtual verifications made the verification process attractive to many more verifiers who had previously been unable to help us. By the end of the week we had allocated every single verification on our books at that time. We also had many verifiers volunteer and, as the geographical limitations no longer applied, we were able to allocate incoming requests to them. This was, to my knowledge, a first for the IBMS – we had never been in a position where we were facilitating assessments as fast as the requests were coming in. The results of this are that these candidates were able to apply for registration far more quickly than previously.

The main differences in the processes are that the portfolio is now reviewed beforehand and the tour is undertaken remotely. In the early stages of implementation of this new process, we recognise that most portfolios will be in hard copy, so we are suggesting that the hard copy is either scanned in, or the candidates can use a template into which the evidence can be uploaded. The only real stipulation we have is that the portfolio is easy to navigate and that, for evidence, the justification and its relationship to the standards is clear.

We have produced several guidance documents and portfolio templates, so please contact registration@ibms.org for further information.

So far, feedback on how well these new processes are working has been very positive. We will continue to collect and collate it and feed this forward in the reviews, which will take place further down the line. I would like to take this opportunity to thank you all for your continued support. IBMS

IMAGES: ISTOCK

MY LAB

FROM INSECTS TO GENOMICS

Ian Davies, Healthcare Science Course Leader at Staffordshire University, gives a guided tour of the campus facilities.

For many of us, university laboratory practicals were where our love for bench science grew. They were an opportunity to apply the academic theory taught in lectures, to learn new skills, and to problem-solve and work with our peers.

We all probably have memories of experiments that worked, and those that didn't. We may remember scribbling results in our lab books and trying to remember exactly which concentration of reagent we had used. We will all remember the feelings we had when we first worked independently on our final-year projects, and the relationships that we developed with the technical staff, our supervisor and our peers.

At Staffordshire University we believe that the learning opportunities that practical sessions provide are invaluable in students' development. They do not just to tie together academic knowledge and practical competence, but are also part of a much wider transition in identity, as students become scientists through enquiry, managing uncertainty, collaboration and autonomy.

Our laboratories opened in 2012 as integral features of our new £30m Science Centre. Designed to provide flexible learning and teaching spaces, they consist of several large open-plan teaching laboratories, each capable of holding 80 students at a time, together with a variety of facilities to support specialist teaching and research. As academics, our teaching covers the breadth of biology and biomedical science from ecology to genomics, and so facilities include everything from an insectary and electron microscopy, to cell culture and genomic sequencing. Students can work within our analytical suite, developing HPLC and GC-MS methods, and collaborate with sports science, psychology, and forensics colleagues to explore experimentation in exercise physiology, EEGs, and ballistics.

For biologists our laboratory is not always indoors, and so our campus also includes a 10-hectare nature reserve with a diversity of habitats, including the River Trent, woodlands, reed marsh, and grassland. Not only does this provide specialist opportunities to study ecological techniques and environmental management, but it gives all our students invaluable opportunities to develop the transferable skills of sampling, identification, and experimental design.

Pivotal to our laboratory teaching are our technical skills specialists, who support staff in the development of experimental ideas, source and prepare equipment for each session, and work with our students to grow their practical skills and confidence. To develop these further, we work hard to enrich practical sessions, for example embedding decision-making, ethical discussions, or quality assurance. As an example, our "virtual" blood bank practical not only allows students to contextualise the theory of antibody-antigen reactions by undertaking bench blood grouping, but also encourages them to consider the practical issues of blood product management, inappropriate requests, and ethical considerations. By not only focusing upon the practical skill, we aim to prepare students for autonomous practice.

With our laboratories in use for undergraduate teaching all week, together with specialist short courses for our MSc students, Healthcare Science Apprenticeship study days, and schools and colleges visiting for our STEM "outbreak" masterclasses, our laboratories are always a hive of activity developing the next generation of scientists. BMS

BECKMAN COULTER

ACCESS ACTIVE-B12

Reliable B12 deficiency diagnosis.

We're more than a supplier – we partner with labs around the globe to deliver innovative, reliable and efficient diagnostic processes and technology.

Providing an early indication of B12 deficiency, the Access Active-B12 provides superior sensitivity and specificity, for improved diagnostic accuracy and greater confidence in patient results.

Trust us to provide accurate diagnoses of anaemia in all its forms.

Elevate your performance. Advance patient care.

Find out more about Beckman Coulter's comprehensive anaemia offering by visiting: **e.beckmancoulter.com/UnitedIn-Anaemia**

#UnitedinProgress


What's causing it
will it get worse
is my diagnosis correct
am I sick
is he suffering a heart attack
which woman is
at highest risk of
cervical cancer
what diseases
do I have
who
should
manage
her heart disease
how can I reduce
my post-operative
hospitalisation costs
who is the best candidate
for treatment
how can we predict
and prevent disease
is something
wrong with me
do I have cancer
am I at risk
is my baby in danger
did my pap miss
something
is he HIV+
will this patient
recover quickly
after surgery
is my baby
healthy
is my treatment
working
can I
still get
pregnant
I know I
am not at risk
we caught it early
I know I am ok
I know the treatment
will work
I am in control
my baby is
fine
I KNOW WE ARE
SAVING LIVES
THE POWER OF KNOWING
Roche Diagnostics gives you
The Power of Knowing that you're
using accurate information to
make the right decisions today,
so your patients can experience
a healthier tomorrow.

Roche