ONE-TO-ONE

STOPPING MALARIA

A look at the vaccine that could cut malaria cases by 40%: *p.16*

MICROBIOLOGY

GUT AND ALZHEIMER'S

What is the connection between gut flora and Alzheimer's?: *p.24*

BRAIN INFLAMMATION

ENCEPHALITIS

A guide to this inflammatory brain condition: *p.32*

THE BIOMEDICAL SCIENTIST

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CONTENTS

IBMS.ORG JUNE 2019

EDITORIAL

NEWS

OPINION

SCIENCE

COVER FEATURE

COVER PHOTOGRAPHY: GETTY

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
(0)20 7880 7556

redactive

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

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ISSN 1352-7673
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PRINTED BY
Warners Midlands plc
The Maltings, Manor Lane
Bourne, Lincolnshire PE10 9PH

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WHAT'S IN A NAME?

The role of the biomedical scientist has evolved, but more work is needed to change public awareness.

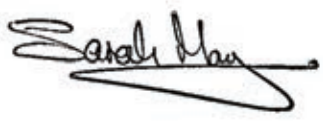
Names are important; having the right name is even more important. Any company launching a new product, or re-launching an established product, will undertake extensive market research to ensure the product name represents the essence and quality of the product. The same is true of jobs and professions: the evolution of the ambulance driver into an ambulance paramedic reflects the repositioning of a role in the public mind to more appropriately reflect the increased knowledge and skills required of the profession.

The role of the biomedical scientist has also changed, but unfortunately the recognition of our profession has not been taken up in the way that it has been for the ambulance paramedics. A close friend of mine is currently involved in a classroom "come as someone who works in a hospital" day and I have been tasked with finding appropriate items. Imagine my shock horror when she said how about a doctor or a "lab tech"? Amazingly, we're still friends, but I can't recall any other outdated title with such enduring tenacity as "lab tech". It seems to be more challenging than the twelve labours of Hercules to embed "scientist" in to the minds and language of anyone outside of this profession.

With Biomedical Science Day approaching, I am about to drag out and dust off my "lab tech" soap box and ask everyone organising a Biomedical Science Day event to use the word "scientist" at every conceivable opportunity. I suppose we do have something to be grateful for and that is that the title "Medical Laboratory Scientific Officer" died a quietly unmourned death. Oh what a curse it was. It brings to mind the words of Lewis Carroll in *Through the Looking-Glass*: "With a name like yours, you might be any shape, almost.".

I want to conclude with a word of warning to all our Biomedical Science Day planners. I once organised a laboratory open day, which I saw as the ideal opportunity to introduce a captive audience to biomedical scientists, their role in cervical screening, and the diagnostic possibilities of a good, cellular fine needle aspiration biopsy.

In my enthusiasm, I totally overlooked the fact that a professional absence of squeamishness is not necessarily mirrored by the general public. I'm not sure if it was my description of a colposcopic biopsy, the sight of me demonstrating an endocervical brush on a brightly coloured plastic cervix or the prospect of an encounter with a loaded biopsy gun, but by the time the second visitor had fainted, I knew it was an open day not to be forgotten – but, unfortunately, not for all the right reasons...



Sarah May
Deputy Chief Executive

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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

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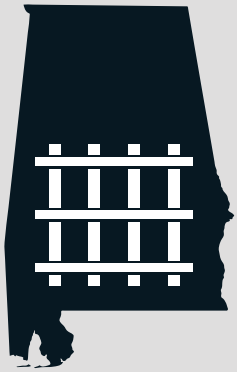
SCIENCE NEWS IN NUMBERS

Bill banning abortion

Alabama lawmakers have passed a bill to outlaw abortion in almost all cases – the strictest such law in the US.

25 votes to 6

The state **Senate approved the law** by **25 votes to 6**, **rejecting** exemptions for **cases of rape or incest**.



16 US states

Restrictions on abortion rights have already been introduced this year in **16 US states**. Under the Alabama measure, **provision of abortion at any stage in pregnancy** would be a **Class A felony**. Doctors could face **10 years in prison** for attempting to terminate a pregnancy and **99 years for carrying out the procedure**.

11 dementia recommendations

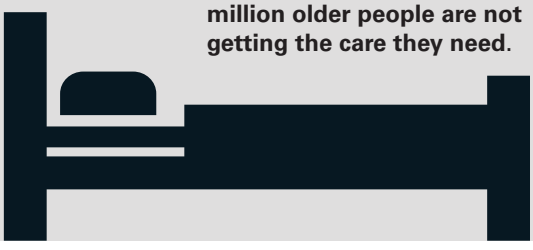
Dementia affects around 50 million people around the world and is becoming more common.

The World Health Organization has launched its **1st ever guidelines** on **how people can help avoid getting dementia**.

They recommend:

1. **Exercise**
2. **Stop smoking**
3. **Eat well**
4. **Don't bother with vitamin pills**
5. **Avoid heavy alcohol use**
6. **Brain training**
7. **Be social**
8. **Keep a healthy weight**
9. **Beware high blood pressure**
10. **Get treated if you have diabetes**
11. **Beware high cholesterol.**

30%



An ageing population

An analysis carried out for Age UK indicates about 30% of areas now have no residential care beds.

While **nursing homes**, which are needed for the most frail, are in an even **worse situation**, with **more than 60% having no places**.

Age UK says the situation is now so bad that about **1.4 million older people are not getting the care they need**.

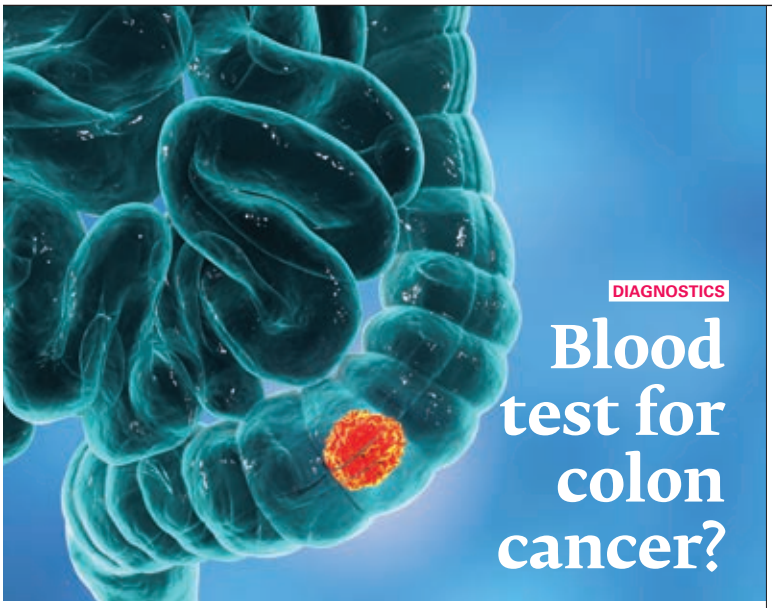
100 PEOPLE

A hundred people undergoing treatment at a UK hospital are to get their DNA analysed in a pioneering trial.

University College Hospital in London plans to invite around **100 people attending its blood pressure clinic** to undergo **genetic analysis**.

The **trial** aims to test how useful such analysis might be in a busy, hospital environment.

Around **85,000 people with rare disorders in the UK** have already had their **genomes sequenced** as part of the 100,000 Genomes Project.



DIAGNOSTICS

Blood test for colon cancer?

If caught early, nearly all cases of colon cancer are curable. However, colon cancer screening suffers from a combination of low compliance rates and over-diagnosis.

Now a group of University of Wisconsin-Madison scientists has identified four protein markers associated with the pre-cancerous forms of colon cancer that are most likely to develop into disease.

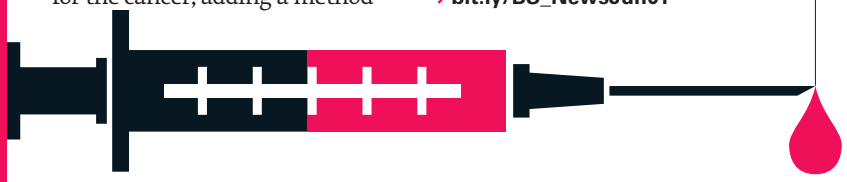
They claim that their findings will ultimately lead to a blood test for the cancer, adding a method to help increase screening rates while reducing over-treatment.

Senior author Bill Dove said: "This study is the first peek at the possibility that there will be blood markers for a minimally-invasive procedure that can reduce over-diagnosis. They do exist."

He continued: "There's good evidence they're being conserved in early disease in humans.

"We didn't expect we could find blood markers for such small, early, pre-malignant polyps in humans, but we did."

→ **bit.ly/BS_NewsJun01**



SCIENCE NEWS

MICROBIOME

ORGAN-ON-A-CHIP BREAKTHROUGH

A research team from Harvard has been able to carry out direct investigations of health and disease-related human-microbiome interactions, using an "organ-on-a-chip".

They were able to culture a stable complex human microbiome in direct contact with a vascularised human intestinal epithelium for at least five days.

The "anaerobic intestine chip" stably maintained a microbial diversity similar to that in human faeces over days and a protective physiological barrier that was formed by human intestinal tissue.

Donald Ingber, study lead, said: "The major paradigm shift in medicine over the past decade has been the recognition of the huge role that the microbiome plays in health and disease. This technology now provides a way to study clinically relevant human host-microbiome interactions at the cellular and molecular levels under highly controlled conditions *in vitro*.

"This method can be used to discover specific microbes that cause disease or that might help prevent conditions."

→ **go.nature.com/2W8fJCe**

VASCULAR DISEASES

SCIENTISTS GROW PERFECT HUMAN BLOOD VESSELS

Scientists have managed to grow perfect human blood vessels as organoids in a petri dish for the first time.

The breakthrough, which is outlined in a new study, dramatically advances research of vascular diseases like diabetes, the team claimed.

They said it identifies a key pathway to potentially prevent changes to blood vessels – a major cause of death and morbidity among those with diabetes.

"Being able to build human blood vessels as organoids from stem cells is a game changer," said the study's senior author Josef Penninger.

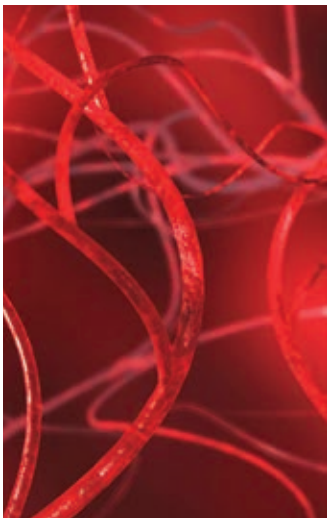
"Every single organ in our body is linked with the circulatory system. This could potentially allow researchers to unravel the causes and treatments for a variety of vascular diseases, from Alzheimer's disease, cardiovascular diseases, wound healing problems, stroke, cancer and, of course, diabetes."

The "vascular organoids" can be cultivated using stem cells in the lab, mimicking the structure and function of real human blood vessels.

When researchers transplanted the blood vessel organoids into mice, they found that they developed into perfectly functional human blood vessels including arteries and capillaries.

The discovery illustrates that it is possible to grow a functional human vascular system in another species.

→ **go.nature.com/2w05RvE**



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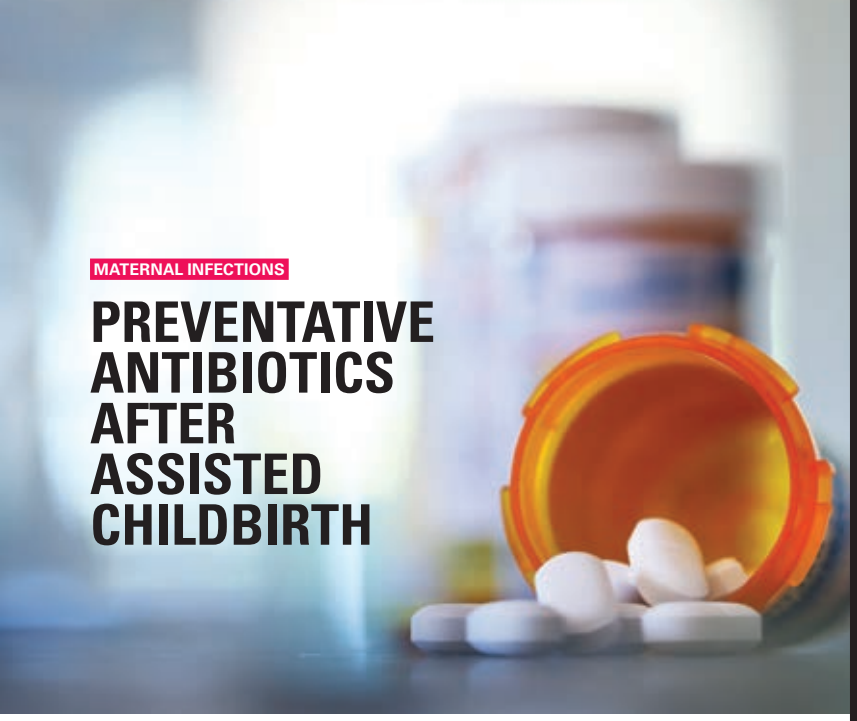


MATERNAL INFECTIONS

PREVENTATIVE ANTIBIOTICS AFTER ASSISTED CHILDBIRTH

Giving a single dose of preventative antibiotics to all women after childbirth involving forceps or vacuum extraction could prevent almost half of maternal infections.

The claim comes from a new paper, which states that this is equivalent to over 7,000 maternal infections every year in the UK.

The first randomised trial of its kind in the UK involved 3,420 women from 27 obstetric units and also found that for every additional 100 doses of antibiotic given prophylactically, 168 doses could be avoided due to fewer post-delivery infections.

This means that a policy of universal prophylaxis after birth could help to reduce antibiotic use by 17%.

Infection rates after assisted vaginal birth without antibiotic prophylaxis are around 16% worldwide, and up to 25% after caesarean section.

For every woman who dies from pregnancy-related infection, another 70 women develop a severe infection.

Marian Knight, from the University of Oxford, who led the research, said: "These findings highlight the urgent need to change current WHO antibiotic guidelines."

→ **bit.ly/BS_NewsJun02**

CANCER TREATMENT

RADIOTHERAPY THAT ROTATES PATIENTS

A new way to deliver radiotherapy that rotates patients in sync with the treatment beam could treat patients with brain cancer as accurately and quickly as the most advanced radiotherapy.

The treatment uses a technique called Dynamic Couch Rotation to carefully synchronise the position of patients with the motion of the radiation beam.

For five patients with brain cancer, scientists calculated the new technique was as accurate as advanced radiotherapy, called Volumetric Modulated Arc Therapy (VMAT).

Harmful or debilitating side effects can limit the benefit of radiotherapy treatment for patients with brain cancer, but the new technique can deliver effective doses of radiation while reducing exposure to sensitive brain tissue nearby.

→ **bit.ly/BS_NewsJun03**

WHAT'S HOT AND WHAT'S NOT

HOT

SNAILS

Japanese researchers have been using CRISPR gene editing technology to make snail shells that coil "the wrong way". Their findings give an insight into the basis of left-right asymmetry in animals.

HOT

COFFEE

Research that shows habitual coffee drinkers are more sensitive to the smell of coffee, could open doors to new ways of using aversion therapy to treat people addicted to substances, such as tobacco.

HOT

TODDLERS

A study reveals that young children learn new words more easily from other children than they do from adults. The findings were presented at the 177th Acoustical Society of America meeting.

NOT

MEASLES

Twenty-five US counties across the country have been identified as most at risk for a measles outbreak due to low-vaccination rates compounded by a high volume of international travel.

NOT

FOOD ADDITIVES

Experts are calling for better regulation of the common additive E171 (titanium dioxide nanoparticles) as research reveals it can impact the gut microbe and could potentially lead to inflammatory bowel diseases.

NOT

MILLENNIALS

Distracted driving is more common among millennial parents than older parents, according to new US research. The work has been published in *JAMA Pediatrics*.

HEART AND CIRCULATORY DISEASES

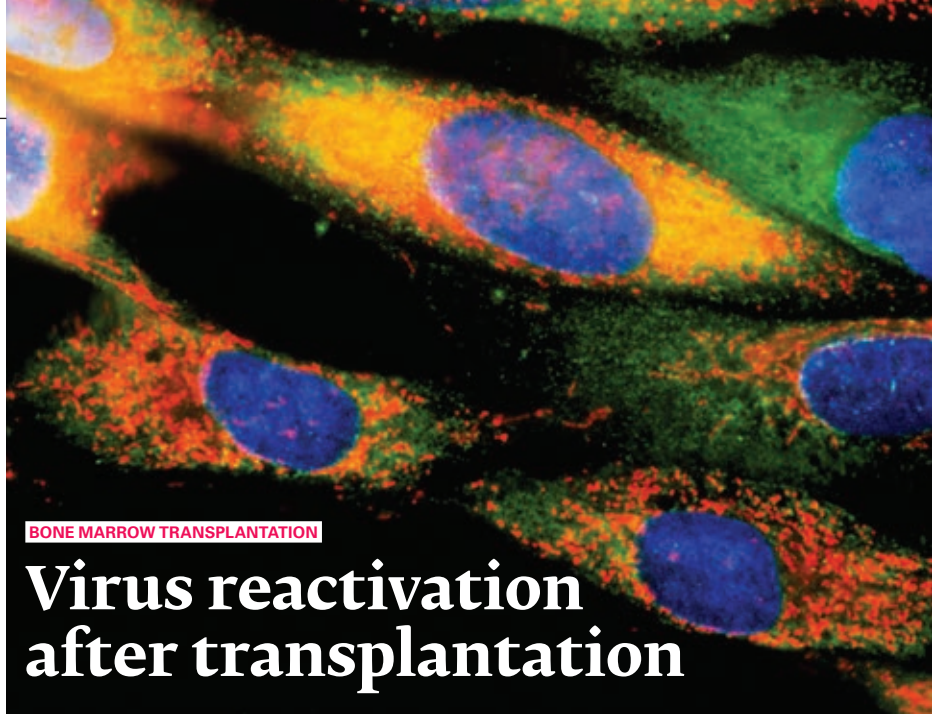
HEART FATALITIES ON THE RISE

The number of people in the UK dying from heart and circulatory diseases before they reach their 75th birthday is on the rise for the first time in 50 years, according to the latest national health statistics.

The figures show an upward trend in deaths since 2014, with 42,384 people dying from conditions including heart attack and stroke in the UK before the age of 75 in 2017, compared to 41,042 three years earlier.

The number of deaths caused by heart and circulatory diseases in under 65s is also increasing, peaking at 18,668 in 2017, up from 17,982 five years earlier. This represents a 4% rise in the last five years, compared to a 19% decline in the five years before.

Simon Gillespie, British Heart Foundation Chief Executive, said: "In the UK we've made phenomenal progress in reducing the number of people who die of a heart attack or stroke. But we're seeing more people die each year from heart and circulatory diseases in the UK before they reach their 75th, or even 65th, birthday. We are deeply concerned by this reversal."



BONE MARROW TRANSPLANTATION

Virus reactivation after transplantation

A new study challenges long-held theories of why a common virus can reactivate and become a life-threatening infection in people with a compromised immune system, including blood cancer patients undergoing bone marrow transplantation.

The research looks at cytomegalovirus (CMV) and used a newly developed mouse model. It is hoped to pave the way for cheaper, safer therapies to protect patients from CMV.

Previous research on CMV reactivation has focused on T cells – the celebrated disease fighters of the immune system.

There had been occasional hints that the antibodies produced by immune system, B cells, played some role against CMV, but it seemed to be a supporting role.

Clinical trials using antibodies to fight the virus were disappointing.

But the new research revealed that strain-specific antibodies made from B cells are responsible for keeping CMV suppressed in mice, without the need for any other immune cells.

A future therapy could work by collecting the CMV-thwarting antibodies from patients who have been exposed to the virus and who are undergoing bone marrow transplant.

The antibodies would be purified and multiplied in the lab, then returned to the patient after transplant.

Dr Geoffrey Hill, paper co-author, said: "This is a big deal for the bone marrow transplantation field.

"Our study shows for the first time that antibodies can play a dominant role in controlling CMV reactivation. This is turning dogma on its head."

→ **bit.ly/BS_NewsJun04**

UNDER THE MICROSCOPE

This month: Wisdom

Wisdom? That doesn't sound very scientific.

Traditionally, wisdom has been discussed in terms of philosophy and religion. Debates around this have been ongoing for centuries. But, over the past couple of decades, there has been an increasing focus on scientific research around concepts of wisdom.

But it's a psychological construct – you can't measure wisdom, can you?

Well, a new paper published in the *Harvard Review of Psychiatry* notes that other psychological concept have been defined and measured, such as consciousness, stress and resilience.

What does this paper say about wisdom?

The authors argue that the basic concept of wisdom has always been the same, suggesting that it "probably has an underlying neurobiological basis". They propose a model of the neurobiology of wisdom, localised mainly in the prefrontal cortex and limbic striatum. They add: "Emerging research suggests that wisdom is linked to better overall health, well-being, happiness, life satisfaction, and resilience."

Can I become wiser?

The paper states that wisdom seems to increase with age, despite the loss of physical health and fertility over time. But there is limited evidence as to whether you can successfully make a conscious effort to become wiser. They add that psychosocial (and possibly biological) interventions that enhance the function of brain areas involved might lead to enhanced wisdom.

What about owls? Why do people think owls are wise?

This is thought to relate to Greek mythology – the goddess Athene, who symbolised wisdom, was often depicted with an owl nearby. The most common theory is that this association was inspired by owls' big eyes and solemn appearance.

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TECH NEWS

SANOFI

VACCINATIONS

Technology could play a role in overcoming barriers to the uptake of vaccinations, argues a new report.

Data, Bots and Drones has been published by the International Longevity Centre UK and supported by a grant from Sanofi.

It states that the use of big data, gamification, the sharing economy and AI, offer opportunities to overcome barriers and counter misinformation and fake news.

The report notes there is now a more savvy online presence and better content to respond to the anti-vaccination movement.

→ **sanofi.co.uk**

NANOCELLECT

DISTRIBUTION DEAL

NanoCellect Biomedical has announced an exclusive distribution agreement with Switzerland-based Bucher Biotec AG.

It covers sales in Switzerland of NanoCellect's WOLF Cell Sorter, N1 Single-Cell Dispenser, consumables and software.

NanoCellect Biomedical is a leader in microfluidic cell sorting solutions for cell-based assays.

Distribution deals outside the US are a "key part" of its growth strategy for 2019.

→ **nanocellect.com**

ANTON PARR

A NEW ADDITION

Tosca 200 is the latest addition to the Tosca series, which now consists of Tosca 400, a large-sample, premium AFM, and Tosca 200, an AFM for medium-sized samples and budget-sensitive research.

Both devices feature the same high level of automation, increasing the efficiency and significantly simplifying the handling of AFM measurements.

Following the introduction of Tosca 400 in 2017 as the first AFM that combined premium technology with time-efficient operation for large samples.

Anton Paar now launches Tosca 200, an AFM for medium-sized samples and budget-sensitive research, but providing the same quality and flexibility.

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THE BIG QUESTION

THIS MONTH WE ASK

"Should a Specialist Diploma be mandatory for band 6?"

Eugene Rees

Ex-Operations Manager, Microbiology
Singleton Hospital, Swansea

In my humble opinion – yes. When Agenda for Change was implemented, one of the biggest and perhaps most unexpected consequences was the "extra" experienced biomedical scientist grade 6. From the unions' standpoint, this was great – looking after their "experienced" members. For managers, however, this was a quandary. What was an experienced biomedical scientist? From my own experience at ground level, it varied; anything from one to three years post-registration, dependant on where you worked. Trainees now tend to do all their training in one discipline and, in theory, someone that attains registration, in a generic portfolio, training in haematology, can be appointed to a band 6 role in another discipline. When shortlisting for band 6 positions, I would always look for relevant experience in the discipline vacant and having the Specialist Diploma was a good marker. A successful Specialist Portfolio is evidence of broad training.

I have performed several microbiology specialist examinations and during pre-examination discussions with the training officer and candidate, I explain to them that the level of knowledge I am looking for is an experienced band 6 person – someone that support workers, trainees and new band 5 staff can go to for advice.

All strong careers need a path with defined, transparent goals – attainment of the Specialist Diploma should be one of the qualifications required for career advancement. Using the it as a mandatory qualification would provide some much-needed standardisation.

Sarah Bruty

Advanced Biomedical Scientist, Haemostasis, and Training Lead for Laboratory Medicine
University Hospital Southampton NHS Foundation Trust

I don't actually think there's a straight answer to this question. It very much depends on the laboratory's circumstances and, on a national scale, laboratories don't have the same job descriptions or requirements for banding.

I think that Agenda for Change missed an opportunity in not having uniform job descriptions across the board. You should be able to have slight variation, but the basics and qualifications required should be decided on a national basis – I think that it is very odd that this didn't happen.

It can cause problems when people move to a job somewhere else, because with their experience and qualifications, they can get a promotion in one place that they can not get in another.

I am strongly in favour of the Specialist Diploma – I think it is an excellent way to evidence specialist training and knowledge, but differing requirements and circumstances mean that it is important that things are not made mandatory. For example, some laboratories have their own systems and sometimes they may find the logistics of completing the Specialist Portfolio hard.

Where I work, there is a real variety. We are able to support people doing the MSc (but I know this is challenging in other locations) and we also do specialist in-house training in our lab.

I think evidencing training is vital and the Specialist Portfolio is one of the best, but should not be mandatory.

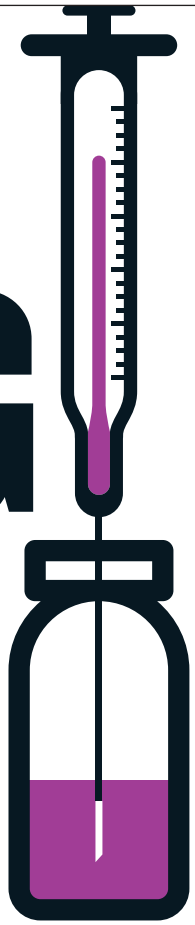
Patricia Fernando

Deputy Manager, Dermatopathology
St John's Institute of Dermatology

Yes – it should be mandatory. As a band six member of staff, if your senior biomedical scientist or manager is out of the lab, then you are the next in line to manage the lab. To do so, you'd either need an MSc or the Specialist Diploma. It's not just about the theoretical side of things, but also about someone's ability around decision making. It is also a solid foundation for other qualifications you can go on to do.

I think that the Specialist Diploma at this level should be mandatory across the board

STOPPING MALARIA



A pilot programme is now underway for a vaccine that could cut malaria cases by 40%. We hear from one of the scientists.

The bite of the female *Anopheles* mosquito is still feared in many parts of the world, for her saliva is likely to be infected with the parasites that cause malaria, which remains one of the most destructive global diseases.

According to the WHO, there were 219 million cases of malaria in 2017, causing 435,000 deaths. While the disease is concentrated in a geographical band around the equator, 92% of cases and 93% of deaths occur in Africa, where it is especially bad in the sub-Saharan region. The money spent on controlling and eliminating the disease in 2017 topped $3.1bn.

Focus on prevention

Treating malaria is mostly straightforward, but the sheer number of infections, coupled with rising drug resistance, means that the focus needs to fix on prevention. For years the key preventative measures against the disease in tropical areas have been insecticide-treated bed nets and indoor insecticide sprays, but the war against the disease took on a new dimension in April with the launch in Malawi of the pilot programme for the first anti-malaria vaccine, called RTS,S. Children up to the age of two will be vaccinated in a drive to reduce the 250,000 childhood fatalities across Africa.

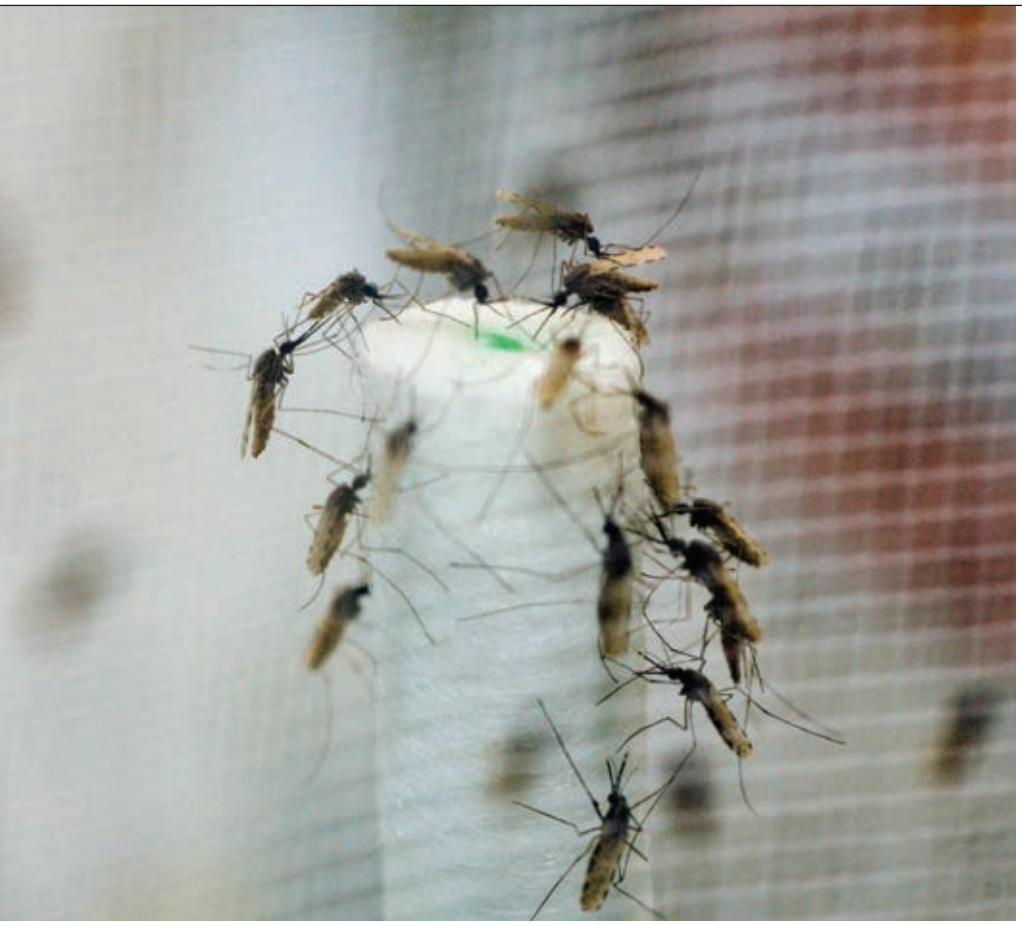
The vaccine is the first ever to target malaria. According to Dr David Schellenberg, Scientific Advisor to the Director of the WHO global malaria programme, the inherent difficulty of devising a vaccine against the disease lies in the complexity of the organism it is combating. "Viruses are relatively simple to deal with," he says. "Bacteria are more complicated, but parasites are several times more complicated again, because there is a lot more genetic material to deal with."

The launch of the vaccine is a significant moment for everybody involved, not least Schellenberg, who has been working on the global response to malaria for the best part of 20 years. "This is probably the longest intervention in the history of malaria," he says. "The vaccine was first developed by scientists back in the 1980s and it has since gone through an extensive clinical development programme with phase 2 and phase 3 trials across seven countries."

Reduction in cases

In 2015 the European Medicines Agency reviewed the data from these trials and subsequently endorsed the vaccine. "As far as they were concerned, the merits of implementing the vaccine outweighed the potential risks," says Schellenberg, "and If malaria was endemic in Europe the vaccine would have been given market authorisation". The next step, though, was the WHO's committee on vaccine safety, which also looked at the data and swiftly recommended that the pilot programme should proceed in Malawi, followed by Ghana and Kenya.

The sense of excitement and satisfaction among all who had



been working on the project for so long was palpable. "It's difficult not to be excited," says Schellenberg. "But some people perhaps got a little too excited. The phase 3 trial showed that the vaccine reduces the number of clinical malaria episodes by about 40%. That's not a perfect vaccine by any stretch. But the existing cornerstone to malaria control is insecticide-treated mosquito nets and they are far from perfect, either, yet the imperfect application of this imperfect tool has lead to dramatic reductions in malaria deaths and disease. When you have a modest proportion of a very large number, that can still be a very large number. If we are able to reduce malaria episodes and deaths by 30-40%, that would be fantastic."

Before the full-scale implementation of the vaccine can happen, the pilots need to iron out any lurking operational issues. "We have to generate experience of deploying the vaccine at scale through routine systems, then we can really understand how we can get four doses of the vaccine to vulnerable children and what the impact is in terms of lives saved."

A project on this scale calls for a high degree of collaboration between the WHO, national governments and the commercial partners. The financing for the programme has come from Gavi, the vaccine alliance; the Global Fund to fight AIDS, tuberculosis and malaria; and Unitaid. GSK, the manufacturer of RTS,S, has donated ten million doses of the vaccine, while the NGO PATH is helping to coordinate the work. "The WHO is also working to support the individual countries' immunisation programmes to introduce the vaccine," says Schellenberg. "That support comes not just from Geneva, but also the regional office in Brazzaville, and the offices in each country. We are also working closely with research groups in each of the countries to evaluate the different aspects of the programme."

Operational feasibility

So with the vaccination pilot underway, how long before we can expect an indication of the outcome? "The full programme is expected to run four years from now," says Schellenberg. "It will be important to finish that because only at the end of the programme will we have the formal estimate of the impact upon survival.

"We know that the vaccine works and the extent to which it works. That has been clearly shown in the phase 3 trials. The questions now are largely around operational feasibility and understanding the real impact in routine implementation. We've had an extensive piece of work going on the past six months or so to look at the evaluation, and in about two years or so there should be sufficient information available to inform further consideration by the WHO policy advisory committee. So hopefully within those two years we should be in a position to say whether it is worth moving forward with a much larger scale application of the vaccine." BMS

DR DAVID SCHELLENBERG

- ✔ Degrees in clinical science and medicine, a diploma in tropical medicine and health, an MRCP(UK) diploma and a PhD.
- ✔ Various research positions include 10 years with the Ifakara Health Institute in Tanzania, where he led malaria treatment and prevention studies.
- ✔ Professor of Malaria and International Health at the London School of Hygiene and Tropical Medicine, 2005-2016.
- ✔ Directed and supported several large-scale research initiatives addressing malaria drug delivery, malaria research capacity building in selected African universities.
- ✔ Served on various task forces and committees to advance the global response to malaria.

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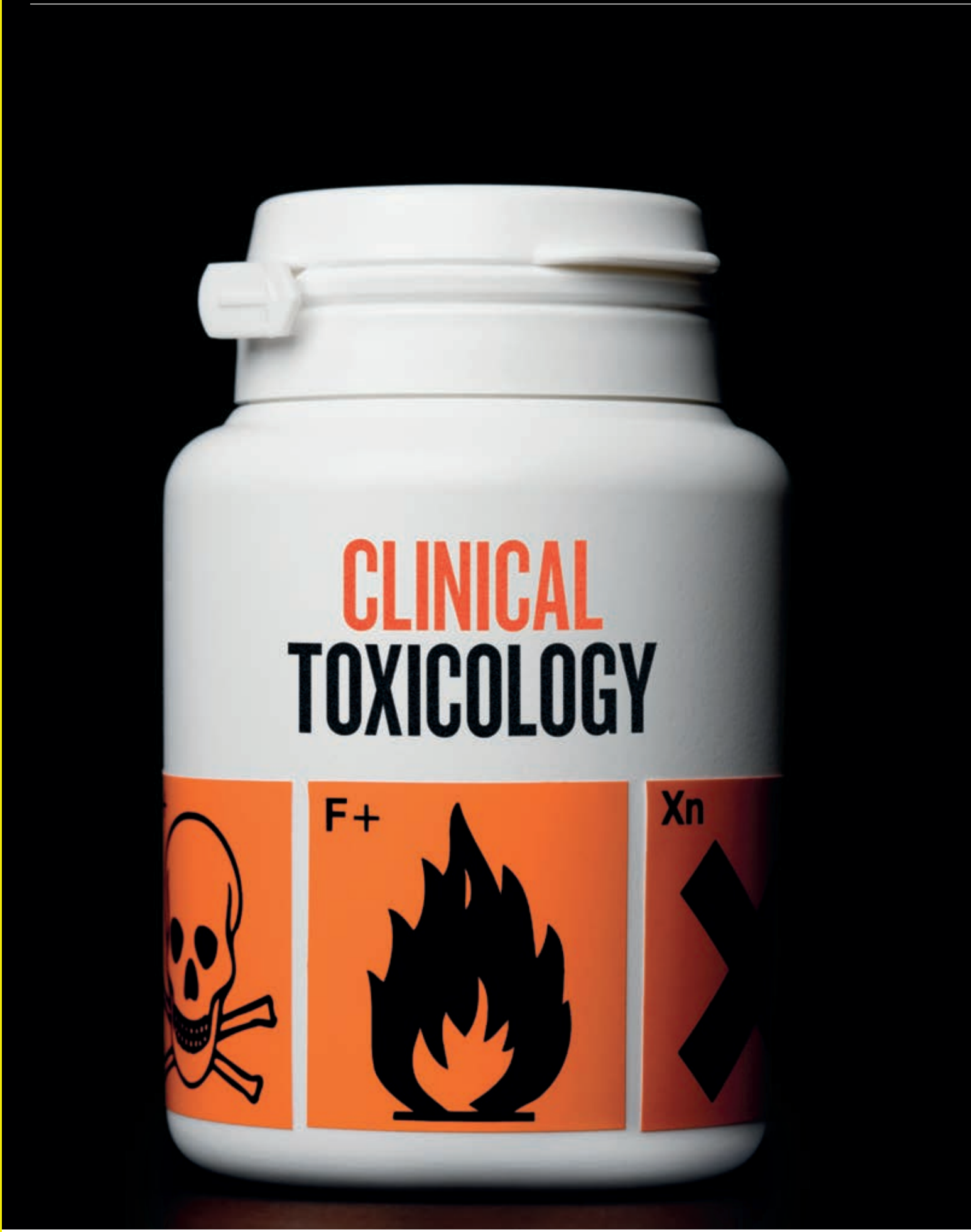

CLINICAL
TOXICOLOGY
F+
Xn

With a **new body formed** that is dedicated to **clinical toxicology**, we ask what comprises the discipline and why it has historically been **under represented**.

As far back as 1500BC, it was documented that hemlock, opium and certain metals could poison enemies and be deployed in state executions. In the well-known example of Plato's account of the death – by drinking hemlock – of Socrates in 399BC, the doomed Senator is advised: "You have only to drink this and to walk about until your legs feel heavy, and then lie down; and it will act of itself."

The discipline of toxicology emerged during the Renaissance and the Age of Enlightenment. For example, Paracelsus (1493–1541) recognised the importance of a dose-response relationship, observing: "All substances are poisons... The right dose differentiates a poison from a remedy." And in 1814 *Traité des poisons* [*Treatise of Poisons*] by Paris-based Dr Joseph Orfila (1787–1853) – regarded by many as the father of modern toxicology – was published. Orfila's lectures were attended by the University of Edinburgh's Dr Robert Christison (1797–1882), and on returning there from Paris, he was appointed in 1822 to the Regius Chair of Medical Jurisprudence and Medical Police (public health).

What is clinical toxicology?

Modern toxicology encompasses three distinct specialties: environmental, forensic and clinical. Environmental toxicology focuses mainly on the harmful effects of chemicals encountered in the atmosphere, the food chain, or occupational/recreational environments, whereas forensic toxicology addresses medico-legal aspects of the harmful effects of chemicals or poisons.

Clinical toxicology, however, is concerned with "the toxic effect of agents whose intent is to treat, ameliorate, modify, or prevent disease states, or the effect of drugs which, at one time, were intended to be used as such."

Dr Stephen Morley is a medical consultant who specialises in clinical chemistry and toxicology at University Hospital Leicester. As well as running a large clinical and post-mortem toxicology laboratory, he also manages patients who present with acute poisonings. "Clinical toxicology," says Stephen, "is a very broad church within, primarily, clinical biochemistry, but with cross-over in haematology, microbiology and immunology. It covers drug assays as well as routine biochemistry and haematology tests, such as liver function tests and full blood counts."

Stephen explains that drug assays range from those that are run in every acute hospital – such as paracetamol, salicylate and digoxin – to drugs that require therapeutic drug monitoring (TDM); these include immunosuppressants, anti-coagulants, and anti-microbial/anti-fungal drugs. "There are also more esoteric drugs," he points out, "that require measurement in overdose cases, but are not available in every hospital. Examples include ethylene glycol and trace elements/metals; and now there is the evolving field of drug compliance, such as anti-hypertensive drug compliance."

Clinical toxicology and other disciplines

As Stephen suggests, clinical toxicology extends into other laboratory disciplines, even those in which drug measurement is not a standard procedure: "For instance, the routine laboratory must be able to perform tests, such as those for liver function, international normalised ratio for paracetamol, glucose for insulin overdose, and full blood counts for clozapine monitoring."

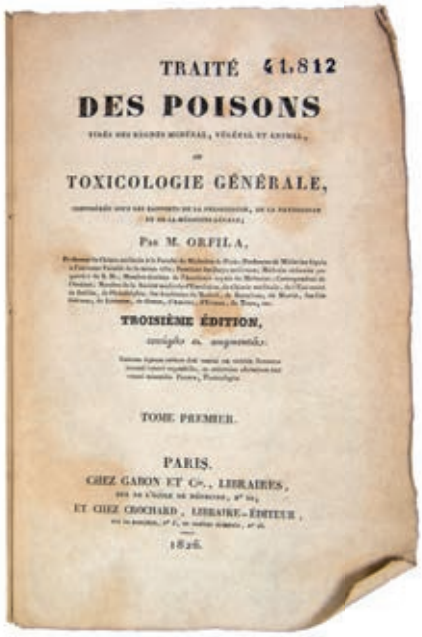
Stephen also observes, however, that although clinical toxicology may be a small part of every clinical laboratory, the discipline is as large as, say, microbiology with regard to the number of patients and staff who may be influenced by the test results: "We are working alongside the National Poisons Information Service (NPIS) to ensure that laboratory testing is fit for purpose, and as part of this we are in the process of updating the NPIS/Association for Clinical Biochemistry and Laboratory Medicine (ACB) guidelines on the laboratory provision for poisoned patients."

Representation of clinical toxicology

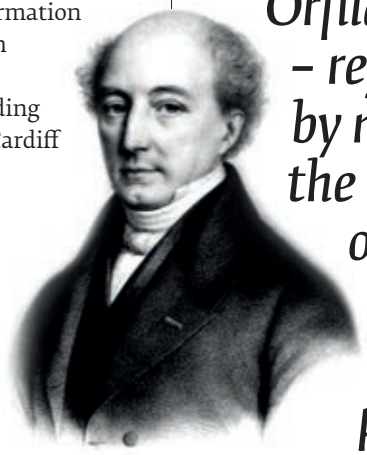
In response to increasing incidents of poisoning in Britain, the 1962 Atkins Report recommended the establishment of poisoning treatment centres and poisons information services. The following year saw the establishment of the Scottish Poisons Information Bureau in Edinburgh, which would later form part of an informal UK network providing similar services in Belfast, Cardiff and London.

Following a review and subsequent management changes in 1996 and 2005, respectively, the UK NPIS now operates from four units in Birmingham, Cardiff, Edinburgh and Newcastle.

A Toxicology Club, which ran from 1971 to 1979, was succeeded by the British Toxicology Society. Its aim is to facilitate discussion of toxicology-related issues throughout all areas of this wide-ranging discipline, and today it has around 700 members.


TRAITÉ
DES POISONS
TOXICOLOGIE GÉNÉRALE,
Par M. ORFILA,
TROISIÈME ÉDITION,
TOME PREMIER.
PARIS,
CHEZ GABON ET Cie., LIBRAIRES,
ET CHEZ CROCHARD, LIBRAIRE-ÉDITEUR,
1826.

In 1814 Traité des poisons [Treatise of Poisons] by Paris-based Dr Joseph Orfila (1787–1853) – regarded by many as the father of modern toxicology – was published.



Historically, however, there has been no single organisation dedicated to clinical toxicology. But now, to fill this void, a new organisation of clinical toxicology professionals – the Clinical Toxicology Network UK (CTNUK) – has been formed.

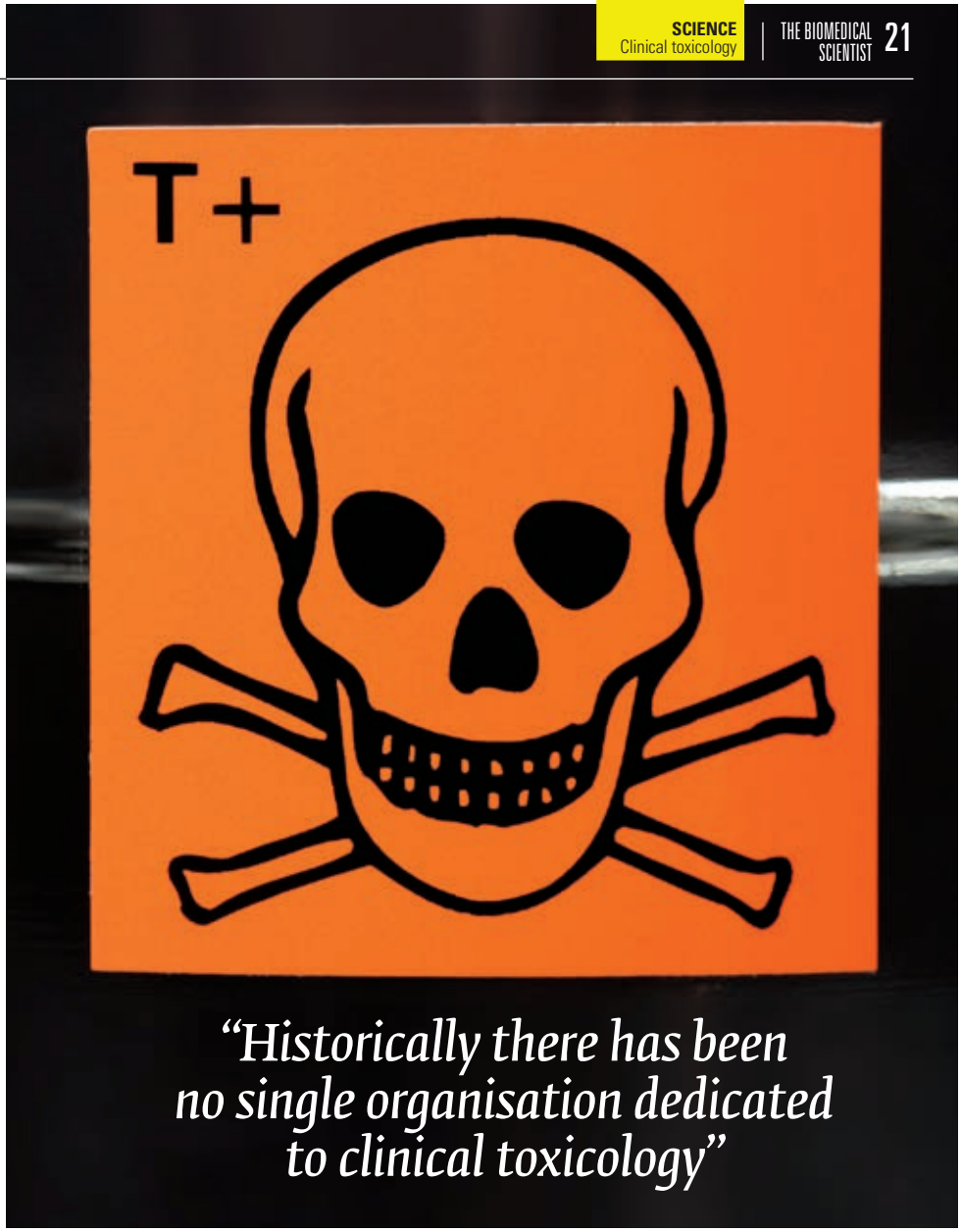
CTNUK

One of the organisation's founders is consultant clinical scientist Dr Alexander Lawson, who specialises in clinical biochemistry and toxicology. Alex, based at Heartlands Hospital, University Hospitals Birmingham, runs a clinical and post-mortem toxicology service and has extensive experience in the development of assays for drug screening and quantitation using several chromatographic techniques with and without mass spectrometry.

When was CTNUK established? "The idea that a group dedicated to the laboratory aspects of clinical toxicology should be established has been discussed between several professionals working in this field for a few years," Alex explains. "We organised the first meeting in February 2018 and have had four more since then. Our meetings are open to all NHS staff working within the field of clinical toxicology. For more information, or if you would like to attend future meetings, please e-mail alexander.lawson@heartofengland.nhs.uk."

Why has clinical toxicology been previously under-represented? "Firstly," says Alex, "there are some organisations dedicated to the field of analytical toxicology – such as the London Toxicology Group and the UK and Ireland Association for Forensic Toxicology – but the focus of these groups is typically targeted at workplace or forensic testing and interpretation, with little time given to the types of clinical analysis routinely performed in NHS laboratories."

Alex explains that clinical toxicology in the NHS may be represented at more general clinical chemistry meetings, such as the IBMS congress or the ACB Focus



"Historically there has been no single organisation dedicated to clinical toxicology"

CTNUK: CURRENT ISSUES OF INTEREST

Topics covered at recent CTNUK meetings have included:

- Cut-offs and methods currently in use for drugs of abuse screening: are these appropriate for clinical use and can they be harmonised UK-wide?
- Coverage of urgent toxicology services listed in the NPIS guidelines
- Evidence behind critical limits for TDM
- The absence of relevant EQA services for important toxicology tests suggest topics for investigation to major research bodies: for example, the National Institute for Healthcare Research and the Human Tissue Authority
- Advise equipment manufacturers on key issues for toxicology and TDM in laboratory medicine
- Provide input into syllabus development in training in laboratory medicine (for example, Scientist Training Programme and FRCPath) and to promote and organise educational/ continuous professional development activities relevant to clinical toxicology.

meeting, but is rarely given top billing, with discussion limited to more general aspects of toxicology: "In general, these groups are not chaired by professionals working within clinical toxicology," he comments.

Alex's second point is that in routine laboratories many people are involved with clinical toxicology but perhaps don't realise it, and if they want to learn more, they may not know who to speak to or which meeting to attend. He further notes that although it may seem specialised, most laboratory professionals working within clinical chemistry laboratories will have acquired some experience of clinical toxicology, whether through performing routine biochemistry or haematology tests on patients who have taken an overdose; measuring anti-epileptic drugs, such as phenytoin to manage their treatment; or screening for drugs of abuse in urine: "We want to encourage staff who take an interest in these areas to attend our meetings," Alex says, "to participate in discussions, share their experiences and take back useful information to their laboratories. Biomedical scientists should have invaluable experience of the numerous analytical issues which may be affecting aspects of their service provision."

Stephen, who is the present Chair of CTNUK, agrees: "The most important message is that CTNUK is for all laboratory staff, from every hospital, and biomedical science staff are likely to be those carrying out the analyses, so they have the experience of what works and what doesn't work on a practical basis. I would encourage as many of them as possible to take an interest in CTNUK."

Providing analytical and interpretative toxicology

What are the main issues that are relevant to the provision of analytical and interpretative toxicology? Alex explains: "In some respects the same things apply to analytical and interpretative toxicology as apply to any aspect of laboratory medicine. We need to ensure that the services offered by laboratories across the UK are of the highest quality. In that respect, one of the aims of CTNUK is to produce and promote consensus guidance for best practice in pre-analytical, analytical and post-analytical aspects of toxicology."

IMAGES: GETTY/ISTOCK/ALAMY

Alex also identifies a need to ensure that there are sufficient resources available for the delivery of urgent, specialised testing for poisoned patients – such as those poisoned by ethylene glycol – and that clinicians, in collaboration with the NPIS, are aware of the most appropriate use of these resources: "All laboratories are concerned with the UK Accreditation Service, and as such we need to identify specialised tests which may need External Quality Assessment (EQA) schemes, or similar, in order to gain accreditation. We also want to learn from each other, with discussion of interesting cases, emerging drug threats – such as New Psychoactive Substances (NPS) – and analytical issues."

Nerve agent attacks and new threats

Two further topics under recent discussion by CTNUK members were the emergency provision of cholinesterase measurement in cases of nerve agent attacks, and emerging new threats and interesting cases.

Stephen expanded on these aspects. "As far as the role of cholinesterase management following nerve agent attacks is concerned," he notes, "NHS laboratories are at present not in a position to undertake testing if there were to be a mass nerve agent attack. The service is primarily set up to support those families where there are problems with anaesthetics, although it can provide support when one-off poisonings occur."

In terms of emerging threats, one issue of primary importance that concerns Stephen is that, with the movement of post-mortem forensic toxicology to private providers, many of the larger centres are investing less in their toxicology services: "There is therefore a potential lack of individuals who are trained in clinical toxicology."

From a clinical perspective, one of the biggest concerns that Stephen has is the ever-changing NPS market: "No NHS laboratory can support or claim to be able to remain up to date with the drugs being used, and so, testing is not happening in the acute scenarios. Although here is a nationally-funded project looking at NPS, the uptake from Accident and Emergency departments to take samples is very poor, so the epidemiology of the problem is not understood."

Continued evolution

The field of clinical toxicology has no shortage of interesting cases. Stephen emphasises that the cases of importance are those which change future practice: "An example of this is a child who was suffering with PICA, a psychological disorder where individuals develop an appetite for non-nutritive substances such as ice, hair, paint and soil. The child was eating paint from the bannisters in his house, and he died from lead poisoning. Although the house had been painted recently, the process had been to just re-paint over existing layers, and, as the house was Victorian, these layers dated back to before lead was banned from paint. The hospital changed it's practice so that every child who presents with PICA is screened for metal toxicity, and several children have been identified as having high concentrations of lead."

Finally, ongoing developments in areas such as molecular-, nano- and computational-toxicology, combined with the establishment of groups such as CTNUK, ensure the continued evolution of clinical toxicology. BMS

AIMS OF CTNUK

CTNUK aims to:

- Produce and promote consensus guidance for best practice, citing evidence where available, in pre-analytical, analytical and post-analytical aspects of toxicology and TDM in laboratory medicine
- Advise on the most effective use of existing tests and the likely utility of new tests
- Provide information for non-specialist laboratories on the selection, application and interpretation of core tests in toxicology and TDM.

POISONING STATISTICS

10

Poisoning ranks among the top 10 reasons for hospital admission in the UK

160,000

Hospital presentations occur annually, as a result of poisoning

2.7m

Last year the National Poisons Information Service provided responses to more than 2.7 million information requests

To view the article with full references, view online at thebiomedicalscientist.net

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

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Sample to Insight

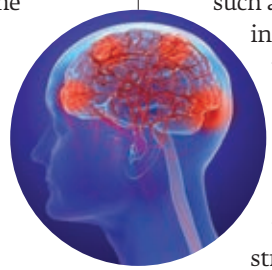
GUT MICROBIOME AND ALZHEIMER'S

Natalia Casey, a Specialist Biomedical Scientist in Microbiology, looks at gut flora and Alzheimer's disease.

In 2015, it was reported that 48.6 million people were living with dementia worldwide and this is set to increase to 75.6 million by 2030. Definitive diagnosis can only be made at post-mortem, so clinical diagnosis is reliant on psychological and radiological assessments. Because of this, research has focussed on the potential uses of serum and CSF biomarkers, such as protein tau and β-amyloid, and the role the laboratory can play in diagnosing dementias, such as Alzheimer's disease (AD). In AD, deposition of β-amyloid protein, known as plaques and neurofibrillary tau protein tangles, are characteristic brain developments, resulting in decreased cognitive function and brain shrinkage by loss of neurons and synapses.

Psychologist William James and physiologist Carl Lange introduced the concept of bidirectional communication and emotional regulation between the central nervous system and intestinal organs in the 1880s. Forty years later, the involvement of the gut microbiota on brain function emerged and the concept of the gut-brain microbiota axis was established.

One of the recent expansions in AD research is the role of gut flora in regulating brain function and modulating neurotransmitters, which can induce β-amyloid deposition and misfolding of tau proteins (tangling) via excessive immune responses. Similar links between the gut microbiota and brain protein function have been implicated in other autoimmune conditions such as multiple sclerosis, and Parkinson's disease. These conditions are also risk factors for the development of dementias.



Gut microbiota

There are over 100 trillion micro-organisms in the gastrointestinal tract and a rich diversity of microbes promotes a robust flora against environmental influences. In an AD patient, reductions in diversity by decreased numbers of anaerobic bacteria, such as *Bifidobacterium, Allobacillum, Akkermansia* and *Firmicutes*, are seen, but data is controversial regarding increases in *Bacteroides*, which thrive on a meat-rich diet. *Akkermansia* reductions are also associated with type 2 diabetes, obesity and increasing β-amyloid protein in the brain.

The microbial diversity can be reduced by external factors, such as antibiotic induced changes, poor diet and medications such as metformin and proton-pump inhibitors. Central nervous system stress can also negatively affect gut flora and change microbial composition. This is via the hypothalamic–pituitary–adrenal axis which is responsive to these environmental factors and releases the stress-hormone cortisol which, when in excess, can increase both gut permeability and damage the blood-brain barrier. The microbiota can interact with the nervous systems by driving immune response, communicating with the vagus nerve and modulating neuroactive compounds.

In terms of neurotransmitter control, organisms such as *Escherichia, Bacillus* and *Streptococcus* species can produce dopamine used in motor control and reward-motivated behaviour. *Lactobacillus, Lactococcus* and *Enterococcus* species release acetylcholine and histamine, which aid sleep, cognitive function and further neurotransmitter regulation. An imbalance of these

IMAGES: SCIENCE PHOTO LIBRARY/ISTOCK

organisms can lead to reduced dopamine and acetylcholine production, leading to cognitive decline via neuronal damage. On the other hand, an increased abundance of gram-negative bacteria can produce excessive endotoxin inducing general inflammatory responses and damaging gut and blood-brain barriers.

Excessive immune activation impairs both the gut and blood-brain barrier, which, in turn, induces neuroinflammation, causes neural injury and ultimately leads to neurodegeneration; a phenomenon that has been termed "inflammaging". An indirect measurement of gut inflammation is the calprotectin stool concentration. This calcium-binding protein can form amyloid oligomers and fibrils closely resembling β-amyloid and another amyloid-associated protein in AD, α-syn. Calprotectin levels in the CSF of AD patients is significantly increased promoting amyloid aggregation, but this is also seen for stool concentrations in 70% of AD patients.

Protein alterations

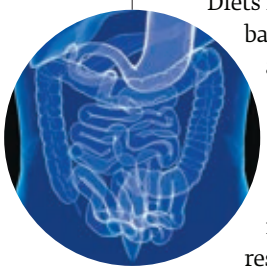
The gut microbiota has been implicated in providing a source of β-amyloid. The most studied bacterial amyloid is curli produced by *E. coli*. These proteins usually help bacterial cells bind to enable biofilm formation and resist immune responses. Similarities between these amyloids and those found endogenously in

the CSF (β-amyloid) have been found, indicating that high concentrations in the gut may strengthen immune responses to amyloid in the central nervous system. Studies in rats have shown that brains exposed to higher amounts of curli-producing bacteria have increased microgliosis, astrogliosis and increased expression of TLR2, IL6 and TNF which can further the inflammatory features of AD.

Bacteria and fungi in the gut can excrete lipopolysaccharides (LPS), which modify gut homeostasis, inflammation and permeability. Predominantly, these arise from abundant gram-negative bacilli and make-up part of a mixture of pro-inflammatory neurotoxins, that when leaked into the circulatory system and cerebral vasculature, have been found to eventually reside in the neocortex and hippocampus, contributing to neurodegeneration. Animal model studies show that LPS injections direct into the brain can result in pathological features, from prolonged elevation of amyloid in the hippocampus, similar to those seen in AD.

Helicobacter pylori associations

Since its first identification in 1982, *H. pylori* gastrointestinal colonisation has been linked to many conditions, including atherosclerosis, hypertension, stroke and peptic ulcer diseases. The vascular disorders are risk factors for AD, implicated by impairing of the blood-brain barrier via inflammatory responses. A Th1 immune response to *H. pylori* infection is characterised by high levels of TNF-α, IFN-γ, IL-2 and IL-12 causing gastric epithelial cell apoptotic damage. As well as the cross-reaction of TNF-α inducing neuronal cell death, TNF-α may also be able to contribute to obstructive sleep apnea, which accelerates amyloid deposition in the brain. In addition, intraperitoneal injection of *H. pylori* in animal models induces memory deficit and increases β-amyloid in the hippocampus and cortex by interrupting synaptic function, just as it can induce tau hyper-phosphorylation creating neurofibrillary tangles.



"Dietary intervention is one of the most effective methods of modifying the gut microbiota"

Microbiota modulation

Dietary intervention is one of the most effective methods of modifying the gut microbiota.

Diets rich with plant-based foods, nuts and antioxidants and low in saturated fats and refined sugars have been shown to inhibit inflammatory responses, reduce insulin resistance and decrease the risk of neurocognitive impairment including AD. This is due to a shift away from *Bacteroides* to increased levels of other anaerobes, including *Akkermansia* and *Prevotella*. Probiotics provide additional support to the microbiota as indigestible substrates act as food for *Bifodobacterium* and *Lactobacilli*, whereas red wine, red berries and green tea contribute to reducing amyloid aggregation and the incidence of amyloid-related diseases. Conversely, diets low in antioxidants and high in pro-inflammatory fatty acids facilitate the deposition of amyloid and activate inflammatory processes.

Faecal transplantation has been used since the 4th century for the treatment of diarrhoea and food poisoning. Nowadays, the NHS provides faecal transplantation services to patients with recurrent *C. difficile* infection with the aim of recolonising the gut. Faecal transplantation has also shown therapeutic potential in neurodegenerative disorders such as Parkinson's disease, which could be expanded to AD to restore gut microbiota diversity and stability. It is thought that this could reduce intestinal permeability and decrease immune activation. Although studies are lacking in this area, modulation of gut bacteria could have far-reaching effects to prevent and delay progression of AD. Donor screening programmes are similar to those of blood donors, with a range of bacteria, parasites and viruses tested and the exclusion of donors with gastrointestinal disease history and use of major immunosuppressives.

The lab role

Due to manufacturing requirements, donor samples are unlikely to be seen in the clinical microbiology laboratory. However, we may see requests for proof of recolonisation or gut microbiome determination as a tool for patient management. For example, in a western diet high in protein and fat in the UK, *Bacteroides* can make up 55% of the microbiome and in North America, this can reach 80%. On a plant-based diet, percentages are tipped towards the *Firmicutes*, which aid digestion of plant carbohydrates and modulate gut inflammation. Implementation of techniques such as RNA gene sequencing will make microbial ecology an exciting prospect for clinical microbiology and for the management of Alzheimer's affected patients. BMS

Natalia Casey is a Specialist Biomedical Scientist in Microbiology, at Weston General Hospital. She is studying for an MSc in Global Health. To see the references, view the article online at **thebiomedicalscientist.net**

ENCODING AND TRANSMITTING DATA

Robert Simpson, IBMS representative on the Royal College of Pathologists Informatics Group, with the latest developments on sharing pathology data.

NHS Digital recently held a workshop with the title "Enabling the sharing of pathology results across the NHS". The major theme of the meeting was to explore how the now static pathology messaging system, which is based on the Pathology Bounded Code List (PBCL), could be replaced with coding and messaging standards and systems to enable pathology data and information sharing across NHS in England.

The aim would be that diagnostic messages and information – for example, a request, a numeric result, an interpretive comment, or a written report – are encoded, transmitted, received and displayed accurately, securely and in a timely manner.

NHS Digital is the national information and technology partner to the health and care system and works closely with similar bodies in Scotland, Northern Ireland and Wales. NHS Digital has been given the job of developing new standards to replace the PBCL and PMIP-EDIFACT and to provide enhancements, which provide greater utility and integration with other NHS electronic data and record systems, such as electronic patient records, public health monitoring, or commissioning and monitoring of service provision.

The NHS Digital workshop, which took place in Birmingham, was convened to bring together stakeholders in the diagnostics – particularly pathology – disciplines to hear about NHS Digital's plans for developments in pathology data capture and messaging.

The IBMS and other professional bodies, including The Royal College of Pathologists and Faculty of Clinical Informatics, together with biomedical scientists from pathology IT departments and IT specialists, industry partners from IT and Laboratory Information System providers and NHS Digital informatics specialists, discussed the work completed so far.

The major theme of the meeting was how the pathology messaging system could be replaced

They also covered the opportunities new systems offer and the challenges of designing and building the replacement systems, implementing them and transferring results and information from old systems, which will be made redundant.

The meeting received confirmation that the use of SNOMED CT as a terminology is endorsed by the NHS National Data Board and that for the message transfer system Fast Healthcare Interoperability Resources (FHIR) is the preferred option. The NHS Digital National Pathology and Diagnostics team described how they are collaboratively developing a data model, a message specification, a SNOMED CT-based NHS-specific catalogue known as the unified test list (pilot projects have already mapped some 350 test names) and a units of measure standard. IBMS

To find out more about this project and how to get involved, visit **hscic.kahootz.com/connect.ti/PathologyandDiagnostics**
NHS Digital will be hosting a free exhibition hall seminar at IBMS Congress this year.

IMAGE: ISTOCK

DISCUSSING THE HEART OF THE MATTER

Dr David C Gaze looks at the history and issues surrounding adopting high-sensitivity cardiac troponin testing.

Cardiac markers have been integral to the diagnosis and management of patients with acute cardiac pathology for over 60 years. In 1954, aspartate transaminase; more common to us now as a part of liver function testing, became the first "cardiac marker", following a small laboratory study of dogs undergoing induced acute myocardial infarction (AMI) by clamping of the coronary arteries.

The main stay of diagnosis of AMI for over 30 years utilised non-specific muscle enzymes (eg creatine kinase [CK]) or myoglobin. These are often elevated in non-cardiac conditions, such as renal failure and muscle pathologies. The advent of cardiac troponin T (cTnT) and cardiac troponin I (cTnI) assays revolutionised AMI diagnosis in the late 1990s.

However, it took a number of years to establish their use in mainstream clinical chemistry. At that time, discreet automated immunoassay analysers were emerging with assays with long turnaround times. These were still far better than analysis of CK isofoms by electrophoresis that took hours to complete, or CK-MB mass assays, often batched twice daily, much to the detriment of the patient lying on a trolley in a corridor in A&E.

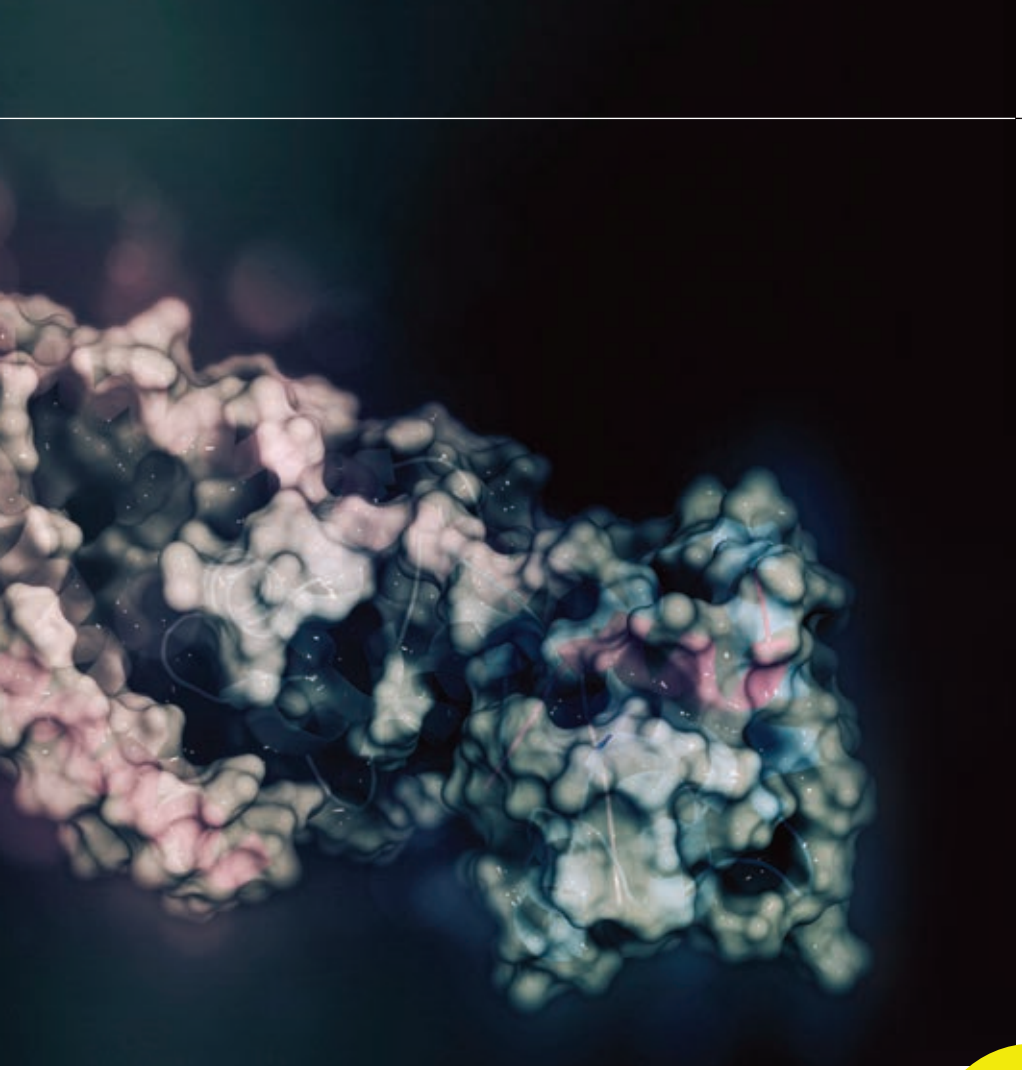
The holy grail

Early troponin assays had a high clinical cut-off for AMI. This was akin to the CK-MB cut point, as determined by the World Health Organization 1979 AMI diagnostic criteria. The early assays were a perfect diagnostic tool, providing a clear dichotomous answer to the diagnosis of AMI. Patients without AMI were troponin-negative. Those with AMI were positive. It was a brilliant test – the holy grail of laboratory medicine.

Patients had to wait 12 hours for diagnosis; only to wait further to find a suitable in-patient bed or to be sent swiftly in the direction of the exit – on foot. For years we basked in the glory no other diagnostic test provided; until HbA1c for diagnosis of diabetes mellitus, but that is another story.

After the halcyon years of the 1990s and the "noughties" it became more apparent that troponin may not be all that it was cracked up to be. As measurement became common with the advent of large throughput immunoassay analyers joined up on tracks, churning out results in as little as 10 minutes, not to mention the significant reduction in cost, anyone and everyone was ordering troponin– and a second, third or fourth troponin if they did not believe the first. A few spanners were then thrown into the works.

The first nemesis was the elevation of cTn in patients with renal failure, followed by a plethora of other non-cardiac conditions demonstrating elevation of troponin in the absence of overt AMI. Furthermore, troponin was elevated in the "healthy" undertaking arduous physical exercise, such as marathon running without what seemed, any detrimental effect. This created clinical confusion and much head



scratching. It also induced brow mopping in industry for fear of potential litigation. For a test we fell in love with, we suddenly became cautious of its utility even fearful of its existence.

Revolutions

Move on a few years and a second cardiac biomarker revolution occurred: the advent of high-sensitivity cardiac troponin (hs-cTn) assay. How could this great test possibly be an even better test? A question asked by many.

Hs-cTn has brought about three main clinical changes. Firstly, the late diagnostic window of six to 12 hours has rapidly shifted downward, with guidelines currently in common practice using an admission and three-hour protocol.

There is also a drive to adopt the use of a zero-two or even zero-one hour protocol and a zero-hour rule-out decision if hs-cTn is below the assay limit of detection. These protocols, however, are still under investigation and have not been universally adopted.

The second revolution was that it became apparent that the fear of clinical false-positives in non-cardiac pathologies was not warranted and many studies demonstrated poor prognosis in those who were troponin-positive in the absence of AMI. The caveat to this is the exercise cohort. Troponin testing has rapidly moved from an AMI event marker per se, to a risk marker representing cardiac cell death. The pathophysiological mechanisms of troponin release in non-cardiac conditions are still a matter of great debate. That said, hs-cTn measurements are determined by immunoassay technology that is somewhat dated. These assays really challenge the performance of instrumentation at the low end, especially separating out background noise from signal generated by antibody-antigen reactions. As with any immunoassy test, troponin assays are not immune (pardon the pun) to analytical false-positive results from exogenous or endogenous substances.

Most notably of late is that of biotin interference. These incidences are relatively infrequent given the number of troponin measurements made daily on a global scale. The savvy scientific or clinical laboratarian should be aware of potential interferences and suspect them when a troponin result does not fit the clinical presentation. Remember – treat the patient and not the laboratory result.

Armamentarium

Thirdly, the distribution of hs-cTn within the reference interval of a healthy population previously deemed of no clinical significance may carry long-term prognostic value. Maybe hs-cTn could become part of our armamentarium of health screening tools in the same way we use cholesterol or C-reactive protein. The value of this has yet to be substantiated, but large epidemiological cohorts are now being studied to identify a potential novel use of troponin measurement.

The utility of hs-cTn measurement has undoubtedly been a success and is of great benefit to patients where early diagnosis equates to early interventions and better prognosis. It is also apparent that there are novel uses of measuring hs-cTn outside of the classical chest pain patient with suspected AMI. There are exciting times ahead where research will rapidly change into routine clinical practice to better serve the patients using our laboratory services. BMS

Dr David C Gaze is a Lecturer in Clinical Biochemistry and Director of Employability at the University of Westminster. He is also Co-Editor in Chief of *Practical Laboratory Medicine*. Dr Gaze is presenting a lecture entitled "High-sensitivity troponin: current guidelines, benefits and challenges" at IBMS Congress at 9am on Wednesday 25 September at the ICC, Birmingham.

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CRISPR/Cas9 Genetic Engineering

CRISPR/Cas9 Genetic Engineering – How Gilson Manual and Automated Pipetting Tools Facilitate the Process

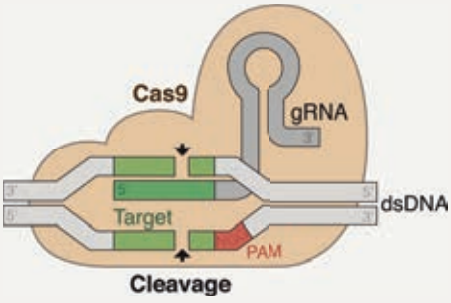
CRISPR/Cas9 is undoubtedly one of the most revolutionary tools in modern molecular biology with wide reaching applications for basic science, industry and healthcare. Within only a few years after its initial discovery as a programmable gene-editing technique, CRISPR/Cas9 has fast become the method of choice for genome engineering in many laboratories all over the world.

Gilson provides scientists with a range of manual and automated high precision liquid handling tools to enable CRISPR/ Cas9 gene editing research. By choosing the right tool for the right job, convenience, productivity, accuracy and precision can all be maximised to ensure reproducible and verifiable results throughout the CRISPR workflow.

As with many techniques in modern molecular biology, CRISPR/ Cas9 workflows are dominated by pipetting, liquid handling and the complexing and delivery of key reagents. Based on Gilson's longstanding expertise in the development of liquid handling and laboratory automation, our products offer the high level of accuracy and precision required for all levels of a CRISPR/Cas9 experimental workflow.

The Gilson PIPETMAN® L Multichannel or new electronic Bluetooth®-enabled PIPETMAN® M Connected Multichannel ranges make setting up multiple 96-well plates for clonal cell culture straightforward and fast, giving you the maximum probability of detecting your modification of interest.

Recent developments in the CRISPR-



Cas9 field are enabling researchers to perform high throughput CRISPR screening experiments; however, with such large-scale workflows, manual sample preparation is often inefficient, time consuming and laborious. The accuracy and intuitive operation of the Gilson PLATEMASTER® give researchers the ability to streamline the workflow of CRISPR/Cas9 studies at scale. PLATEMASTER® is the ideal solution for performing 96-well or 384-well plate-to-plate transfers or for transferring buffers or media from a reservoir. With zero programming, minimal set-up is required, and its small footprint makes it ideal to use in a laminar flow hood or cabinet

For the sample preparation and qPCR validation of clones, the Gilson PIPETMAX® automated liquid handler removes the risk of manual error. With its volume range from 1 µL to 1 mL, and the ability to use 1 to 8 pipetting tips at any one time, PIPETMAX® is the most versatile liquid handler for its size. PIPETMAX® can eliminate user to user error, as well as human error in sample transfers, while completing experiments unattended, leaving scientists more time to focus on more important tasks. The ability to use 96- and 384-well plates, allows for increased throughput with sample tracking. PIPETMAX® uses the same tips as the manual Gilson pipettes so you can be assured of the same excellent performance.

In addition to the PIPETMAN® L and PIPETMAN® M manual and electronic pipettes, PIPETMAX® offers industry-leading accuracy and precision and is the perfect accompaniment for automating your qPCR validation experiments. The Normalization Assistant, a software wizard, allows you to import your DNA concentrations: PIPETMAX® automatically calculates the volumes required to be transferred to create your normalized plate. In addition, the qPCR Assistant, also a software wizard, helps you to set up your qPCR experiment exactly how you want it and keep track of numerous samples with ease. Its flexibility allows you to create and store multiple experiments and use our preferred labware, while creating an output file that can be imported directly to your thermocycler.

For further information, download the full Tech-Note on CRISPRCas9 Genetic Engineering at go.gilson.com/CRISPR-TN or visit www.gilson.com

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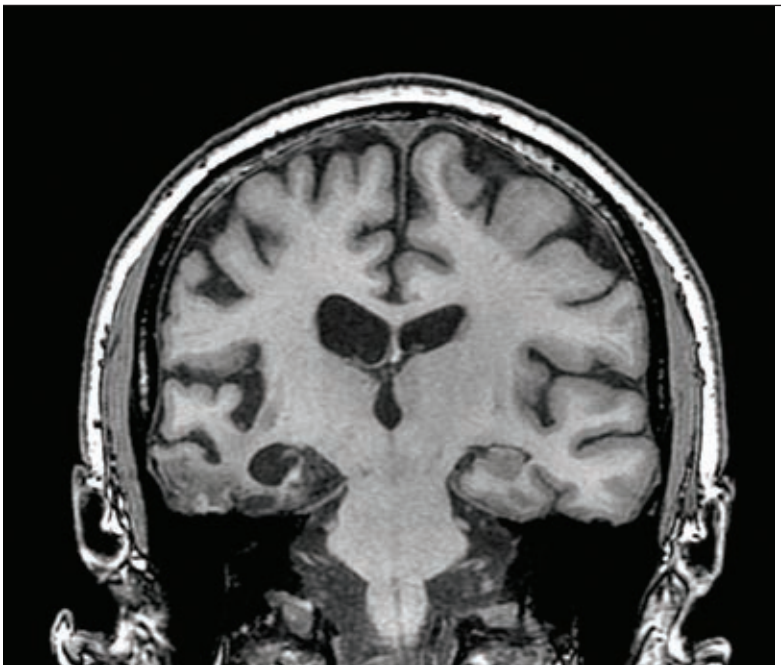


WHAT IS ENCEPHALITIS?

A nuts-and-bolts guide to the inflammatory brain condition, by **Dr Ava Easton**, the Chief Executive Officer of the Encephalitis Society.

Encephalitis is simply inflammation of the brain. It can be caused, in very broad terms, one of two ways: either through an infection (ordinary, everyday infections, such as the flu, herpes simplex and measles, among others) breaching the blood-brain-barrier and mounting a direct infectious attack on the brain, or through a person's own immune system detecting something it considers unfamiliar (these might be tumours, or proteins in the brain), and the immune system attacking the brain in error.

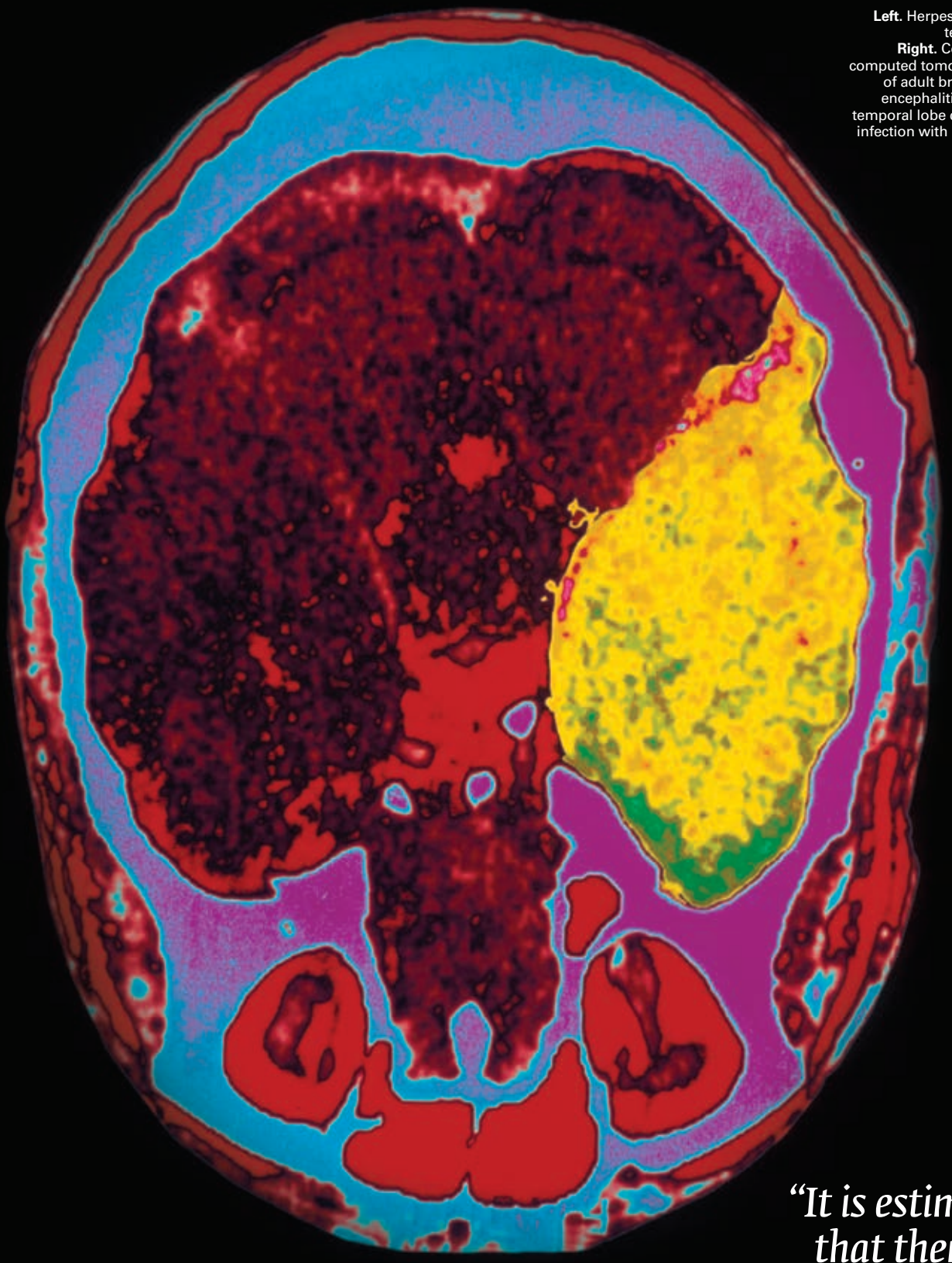
Infectious and autoimmune encephalitides can, however, present in very different ways. Infectious encephalitis often has a very rapid onset, while autoimmune encephalitis can present over days, weeks and in some cases months. These, as we will go on to illustrate, can have important consequences for patients.

Global incidence figures are difficult to ascertain, due to variations, such as geographic distribution of causative agents, immunisation policies of different countries, and methodological issues, such as how cases are defined, diagnosed and recorded. It is estimated that there are around 500,000 cases a year worldwide: one person every minute. This is likely an underestimate. Add to this the fact that in many countries encephalitis has a higher incidence than motor neuron disease (MND or ALS), multiple sclerosis (MS) cerebral palsy, and bacterial meningitis, then it seems anomalous that despite these conditions being less

KEY MESSAGES

- Encephalitis (inflammation of the brain) is a serious and often devastating neurological condition.
- Encephalitis can be caused by infection or by a person's own immune system.
- Brain imaging and lumbar puncture are critical to diagnoses.
- Patients can be left with an acquired brain injury and will need ongoing therapeutic treatment and support.
- The Encephalitis Society is a source of support and information for patients, families, those left bereaved and professionals involved with the condition.

IMAGES: SCIENCE PHOTO LIBRARY/ISTOCK



Left. Herpes encephalitis temporal lobe
Right. Coloured axial computed tomography scan of adult brain, showing encephalitis in the right temporal lobe caused by an infection with herpes virus.

"It is estimated that there are around 500,000 cases a year worldwide: one person every minute"

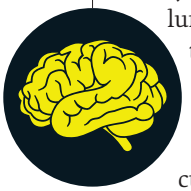
common, they receive a much higher clinical and public profile than encephalitis. Independent polling commissioned by the Encephalitis Society tells us that around the world still eight out of 10 people have not heard of the condition.

Mortality is higher than many other neurological diseases, and may be even more so in low- to middle-income countries, particularly where vaccination programmes do not exist for preventable forms of the condition, such as measles encephalitis and Japanese encephalitis.

Diagnosis and treatment

Diagnosis of encephalitis is often considered a diagnosis of exclusion. Patient history is important: pre-existing conditions that might affect immunity – for example, HIV; history of mental health, drug or alcohol abuse; or exposure to infections, such as measles, mumps or chickenpox. Also, have they travelled out of the country recently (could they have been bitten by ticks or mosquitoes that may have been carrying infection)? Or, through their occupation, could they have been exposed to toxins or chemicals?

Bloods will be taken for blood and serum testing and patients are usually tested for HIV. Brain imaging and lumbar puncture are perhaps the two most important elements in reaching an encephalitis diagnosis – looking for evidence of brain inflammation and of current or recent infection. Testing of serum is important because of autoimmune causes. In some cases, where diagnosis is proving difficult, a brain biopsy may be conducted.



Diagnostic and management guidelines for infectious causes exist for various countries and guidelines for autoimmune causes are in development.

Where infectious types of encephalitis are suspected, a drug called acyclovir is administered, often as a precaution (it is critical in the treatment of a herpes encephalitis). Antibiotics will be given if bacteria are suspected, however, viral causes are much more common. Fungal and parasitic causes are also a possibility, but rare. Other infectious causes generally have to run their course and are reliant on the patient's immune system.

Patients who have an autoimmune cause are treated with a range of immuno-modulatory therapies, such as high-dose steroids, immunoglobulin and plasma exchange. Autoimmune patients are at risk of relapsing disease and sometimes second-line therapies, such as rituximab and cyclophosphamide, are introduced as part of their treatment plan. Where there is an underlying cause, such as a tumour, it will need to be removed or treated to inhibit the immune system response.

Outside of this, treatment is symptomatic and typically involves standard nursing care: ventilation, monitoring of consciousness and respiration, sedation, anti-convulsants, and treatments to address secondary infections along with keeping the patient hydrated.

One particular element that complicates diagnosis and treatment is the two diverse ways that infectious and autoimmune encephalitides can present. In particular, autoimmune encephalitis can present as psychiatric in nature and these patients can go down psychiatric pathways, in some cases for weeks and months, before something occurs in their presentation, that may raise a neurological red flag. Understandably,

ENCEPHALITIS SOCIETY

Although based in the UK, the reach of the Encephalitis Society is worldwide. The vision of the Encephalitis Society is a world aware of encephalitis, its consequences and the support available. Its mission is to increase global awareness of encephalitis, saving lives and building better futures, and it works to improve the quality of life of all people affected directly and indirectly by encephalitis, by providing support and information for patients, families and professionals, by raising awareness (its primary driver in this is World Encephalitis Day on 22 February each year), and by funding and collaborating on research into the condition. It's work is evidence-based, peer-reviewed, benefits from a world-renowned scientific panel and has won numerous awards, including two highly commended from the British Medical Association and Charity of the Year.

SYMPTOMS OF ENCEPHALITIS

Reprinted with kind permission: Encephalitis Society

Infectious encephalitis	Autoimmune encephalitis
• Flu-like symptoms • Dizziness • Malaise • Headache • Vomiting/gastrointestinal upset • Fever. **Later stages indicating a more serious illness involve lowered consciousness which may include:** • Confusion/drowsiness/seizures/coma. **Other symptoms may include:** • Photo-sensitivity/sensory change/inability to speak or control movement • Uncharacteristic behaviour.	**Symptoms will vary depending on the particular autoimmune cause but may include:** • Confusion • Altered personality or behaviour • Psychosis • Movement disorders • Repetitive, involuntary motor or vocal tics • Seizures • Hallucinations • Memory loss • Sleep disturbance.

this can have a significant impact on outcomes both physically and psychologically for patients.

Outcomes and quality of life

Whilst some people may make a good recovery, the long-term consequence of encephalitis for many is life-changing and results in an acquired brain injury. The consequences of which can be cognitive, physical, behavioural, emotional and psycho-social. People may experience changes in their view of themselves (or their relatives). This is both fuelled and exacerbated by memory problems, changes in personality, feeling different, and loss of emotions, thoughts or behaviour. Returns to work and education can result in repeated failure in some case and with this comes additional challenges with mental and emotional well-being.

The range of outcomes can be wide-ranging, and rates of recovery in survivors less than for some other forms of acquired brain injury. This latter point can be in response to a range of issues (such as challenges in understanding and making sense of a condition most people have never heard of; a lack of collective understanding in people's social circles and communities in relation to the outcomes of the condition; and as a result of being discharged often more quickly than other brain injury groups because encephalitis survivors rarely have the orthopaedic or physical injuries that accompany some other forms of brain injury) and has direct consequences for quality of life post-illness. Neuropsychology and neuropsychiatry are often critical interventions in the recovery of patients post-encephalitis. BMS

Dr Ava Easton is the Chief Executive Officer of the Encephalitis Society and an Honorary Fellow at the Department of Clinical Infection, Microbiology and Immunology, University of Liverpool. To view the article with full references, visit **thebiomedicalscientist.net**

CASE STUDY: LIFE HAS CHANGED DRASTICALLY

Tricia describes Maddilyn's journey with an autoimmune encephalitis: anti-NMDA-receptor encephalitis.

Maddilyn was a typical five-year-old: silly, loud, full of energy, and a bit sassy. She had always been a kind and affectionate child. She was helpful and mindful of others, until one day she wasn't.

Suddenly, Maddilyn became sarcastic, aggressive, and combative. Everyday things became a struggle. Our bright, silly, carefree dreamer had morphed overnight into an angry, moody, sad child. Her father and I attributed her change in behaviour to the stressors in life: starting school, family illness and the addition of a new sibling. But when the behavioural interventions we normally used stopped working and her behaviour escalated into violence, while at the same time she refused to eat or sleep, we knew something more was wrong.

On 17 May, 2016 after months of aggressive behaviours, refusing to eat, endless sleepless nights, and no answers, she suffered a seizure and was given the diagnosis of anti-NMDA receptor antibody encephalitis.

A quick search of the internet left me feeling overwhelmed. I learned that NMDA is treatable and that outcomes are good with early diagnosis. It was unclear at what point in the disease Maddilyn was, but her titres were apparently excessively high. She was immediately started on IV steroids and intravenous immunoglobulin and within hours she was awake, smiling, and asking for food for the first time in two weeks.

She has had multiple drugs and therapies, and is better in many ways, but at the same time, not better at all. Since diagnosis, Maddilyn struggles with managing a variety of symptoms: headaches, fatigue, nausea, random pain and blurred vision, she struggles to formulate thoughts, remember things; she struggles with focusing attention and controlling impulses. She has mood swings, is often anxious, and is easily overwhelmed by stimulus.

Our life as a family has changed, drastically. Maddilyn has a central line that requires daily care. She no longer has independence to shower and requires help. She has weekly infusion appointments that sometimes take the whole day. She's hospitalised every other week for treatment. Medications changed her physical body. She has lost the innocence of childhood, because she has seen and been through far more than any child should. As her parents, we have lost the blind ignorance that allowed us to sleep at night. We live on the edge of anxiety and analyse every behaviour for signs of relapse. Raising awareness of the condition has been a huge part of Maddilyn's treatment and our healing.

Case study adapted and reprinted with kind permission of Encephalitis Society

BIOMEDICAL SCIENCE DAY ACROSS THE FOUR NATIONS

As part of this year's **Biomedical Science Day** celebrations on **Thursday 20 June**, we have asked a hospital in each of the four nations to take the lead in promoting the excellent work of our profession. Each hub will showcase a laboratory and inform the public, patients and other hospital staff about their work at the heart of healthcare.

Northern Ireland

Royal Victoria Hospital will be launching its brand new cellular pathology laboratory. Joined by IBMS President Alison Geddis and IBMS Chief Executive Jill Rodney, Governance and Quality Manager Shauna McAuley will lead a tour to showcase the new laboratory to a select group of VIPs and media and then the tours and celebrations will be open to the wider public.

Shauna said: "For Biomedical Science Day we are going to be introducing our new cellular pathology laboratory and service. The Belfast trust cellular pathology department is the amalgamation of Belfast City Hospital and Royal Victoria Hospital cellular pathology services into the newly-refurbished Institute of Pathology on the Royal Victoria Hospitals site. The cellular pathology department implemented a new managed equipment and service contract in June 2018 to maximise a Lean working model, providing smart automation, rapid processing and specimen tracking.

"The department will also be introducing digital pathology towards the end of 2019. This modernisation ensures that the highest quality pathology support is given to the clinical teams managing patient outcomes."

Alongside the laboratory's launch, Royal Victoria Hospital will be bustling with biomedical science activities. They will be presenting their Spirit of Biomedical Science Award, presenting a series of "a patient I'll never forget" lectures, hosting a Harvey's Gang stand and supporting a "living labs" stand in the foyer.

If you're based in Belfast, don't miss the opportunity to join in the celebrations. It promises to be one of the biggest promotions of biomedical science yet.

Scotland

Almost a decade into Scotland's 2010-11 drive to consolidate their cervical screening services into a network-based consortia, University Hospital Monklands will be showcasing how the model has enabled the adoption of new technologies and facilitated a national managed service contract for the delivery of services.

IBMS Deputy Chief Executive Sarah May will attend a special laboratory tour for VIPs and media and then the tours and celebrations will open to other professional groups.

The tours will focus on following a sample through the full cervical screening process, revealing biomedical science at work.

IBMS President Elect, Advanced Practitioner in Cervical Cytology and Senior Chief Biomedical Scientist at Monklands hospital, Allan Wilson, said: "Biomedical Science Day is a great opportunity to celebrate the role of our profession in healthcare. Here at

Monklands, our consolidated screening programme has been a great success and we look forward to raising awareness of screening services and encouraging more women to attend."

If you're based in Airdrie, make sure to check in with the cellular pathology staff and see how you can get involved in the wider celebrations going on in Monklands hospital on the day.

England

Six months on, we are going to celebrate the role of the world's first fully digital pathology laboratory at St James's University Hospital, Leeds. The laboratory has now scanned over 250,000 slides that contain up to 200,000 dots per inch (DPI). If printed at a mere 300 DPI, these images would be the same size as a tennis court. The step-by-step process that each slide goes through has been rigorously tested and received ISO15189 accreditation, laying the foundations for national guidelines on using and implementing digital pathology.

IBMS Executive Head of Marketing and Membership Lynda Rigby and IBMS Council member Joanna Andrew will be joining Chloe Knowles, Biomedical Scientist lead for Digital Pathology at St James's hospital, who will be heading a VIP tour of the laboratory and discussing the future of digital pathology, how going digital is a huge change management project and how it is the wider laboratory workforce who make it succeed or fail.

She said: "Implementing digital pathology is a good opportunity to streamline the entire laboratory workflow to make it more efficient. Looking at the laboratory workflow from start to finish can identify areas that can be leaner, and eventually absorb the additional time and free up the resources required to scan slides. A good example is slide archiving and retrieval, and MDT preparation. Pathologists can have instant access to an image for an MDT, instead of waiting for the glass slide to be retrieved from file. This has a direct effect on laboratory staff who file slides, as their time can be used more efficiently for other tasks in the laboratory. It also has benefits for the multidisciplinary team meetings, as more time can be spent discussing individual patients' needs." Alongside the tour of the laboratory, St James's hospital will be hosting a stand in the foyer with a host of activities including virtual reality tours, digitally scanned images of vegetables and a sock chromosome game.

Wales

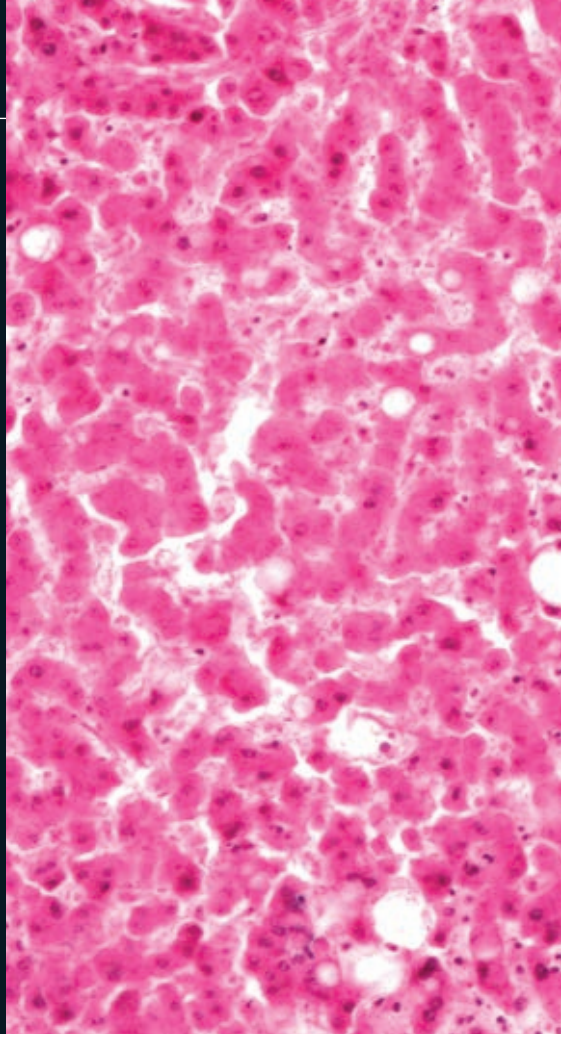
University Hospital of Wales will be launching its brand new biochemistry laboratory. Joined by IBMS Deputy Head of Education Jocelyn Pryce and IBMS Council member Helen Archer, staff will be leading a launch tour for VIPs and media to showcase their new and existing facilities. The tours and celebrations will then be opened to the public, patients and other healthcare professionals.

Nigel Roberts, Laboratory Service Manager for Medical Biochemistry, Immunology and Toxicology, is proud to be on the ground at one of the four Biomedical Science Day hubs and is looking forward to opening the laboratory doors to a curious public.

He said: "We are looking forward to promoting and celebrating the valuable work that biomedical scientists and other laboratory staff put into supporting clinical teams in the treatment and diagnosis of patients, and showcasing the excellent work we undertake for the NHS in Wales. We are also promoting biomedical sciences as an alternative NHS career choice to medicine and nursing."

University Hospital of Wales will also be hosting stands in the atrium, "follow the sample" laboratory tours for schools and some "come and meet a scientist" Q&A events. If you are based in Cardiff, make sure you get involved and show your support. BMS

If you want your department or hospital to celebrate Biomedical Science Day, but don't know where to start, there are lots of event ideas and resources for you at BiomedicalScienceDay.com



British Journal of Biomedical Science, Issue 2 2019 – a synopsis

Editor **Andrew Blann** outlines the content of the Spring issue of the journal.

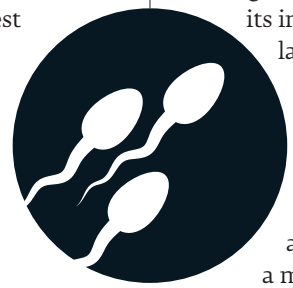
THE LIVER

This issue kicks off on pages 53-58 with a cohort study from China of 1527 patients with non-alcoholic fatty liver disease (NAFLD) and the likelihood of urolithiasis (kidney/bladder stones). Their primary result is that NAFLD is linked to obesity and serum uric acid (perhaps unsurprisingly), but also to the ratio between asparate transaminase to platelet count (APRI), pointing to the use of these markers in diagnosis. Elalfy *et al* from Egypt also studied NAFLD (pages 101-103), reporting high titres of anti-smooth muscle cell antibodies in over half of their 124 patients that were linked to high serum gamma-globulins, a histological activity index, liver fibrosis, NASH score and steatosis.

Focus on the liver continues on pages 64-69 with the study of Arafa *et al* from Saudi Arabia of 70 patients with cirrhosis, 70 with hepatocellular cancer (all of whom had hepatitis C infection) and 70 controls. Their main finding is that certain SNPs in a DNA-repairing gene called *XRCC1* are linked to the presence of the cancer. We may speculate that this association is causative, a hypothesis that can only be answered with long-term follow-up studies, probably lasting decades. A further paper of interest to hepatologists by Al-Radaideh and colleagues from Jordan (pages 70-76), who looked at the percentage of hepatic fat, as defined by magnetic resonance imaging, of a cohort of 156 healthy subjects. They found that hepatic fat levels were linked positively to waist and hip circumference, BMI, leptin, resistin and trigylcerides, and inversely with adiponectin. This study provides the essential physiological data required by pathological studies.

ANDROLOGY

Two short papers are of interest to andrologists. There are numerous risk factors for male infertility, such as pituitary pathology, and others include testicular trauma and genetic abnormalities. Eslaminejad *et al*, from Iran, report on pages 98-100 of a link between an SNP in the gene for bone morphometic protein 4 and low serum levels of this molecule, in 100 infertile men compared to 126 fertile men, suggesting that this gene and/or its product may be useful in diagnosis. Shabani and colleagues, also from Iran, in a study of similar design on pages 86-88 of 185 infertile men and 200 fertile men, show that an SNP in glial cell-derived neurotrophic factor, a molecule important in spermatogenesis, is linked to azoospermia and asthenospermia, but not to oligozoospermia.



IMMUNOCYTOCHEMISTRY AND MOLECULAR PATHOLOGY

Although molecular genetics continues its inexorable progress in medical laboratory science, traditional techniques still have their place. *BRAF* mutations are present in numerous cancers, and can be detected in tissues with an appropriate DNA probe, a method which is expensive

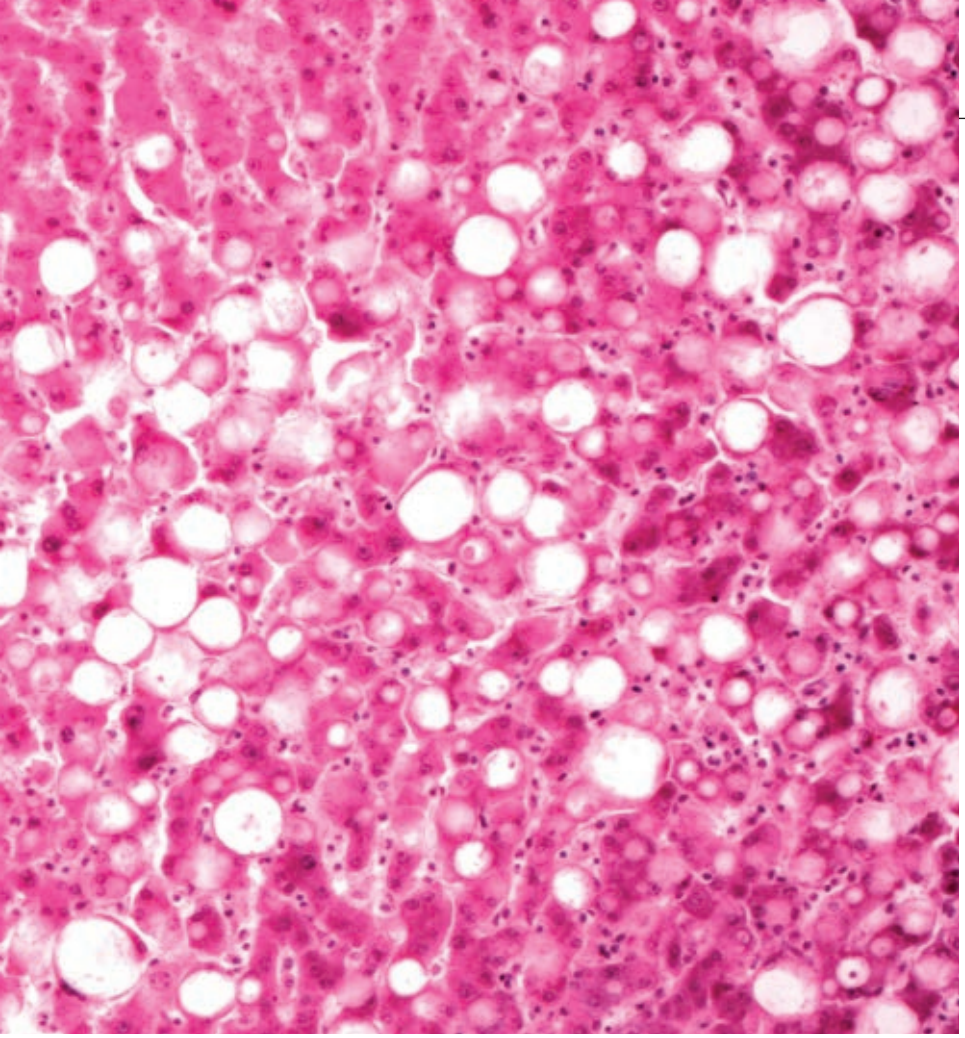


IMAGE: SCIENCE PHOTOLIBRARY

Left. Light micrograph of fatty liver disease (steatosis) near the central vein (zone 3)
Below. Immunocytochemistry of nodular melanoma showing strong staining for BRAF V600E.

and slow. Orchard and colleagues show in pages 77-82, in a study of malignant melanoma, that immunocytochemistry has 100% specificity for the cancer, and is both quicker and cheaper. The former is important because a rapid result is highly desirable so that, if needed, treatment of this disease can proceed as soon as possible. However, two other papers demonstrate the value of molecular genetics. Aminian *et al*, from Iran, show in pages 83-85 that a functional genetic variant in a long non-coding RNA (lncRNA) confers a risk of gastric cancer, a malignancy most often linked to *Helicobacter pylori*. The mechanism is that the lncRNA acts on second messenger and tumour suppressor p27, that itself part-regulates the cell cycle. Thus this particular lncRNA may part-regulate p27, the consequences of which could include inappropriate promotion of a potentially malignant cell. There are several genes with links to breast cancer, the principles being *BRCA1* and *BRCA2*, although there are others known and yet to be discovered. Maroufi and colleagues report, on pages 89-91, no differences in SNPs in genes for IL-27 and IL-33 in 140 women with breast cancer compared to 140 healthy women, thus excluding these SNPs from further studies.

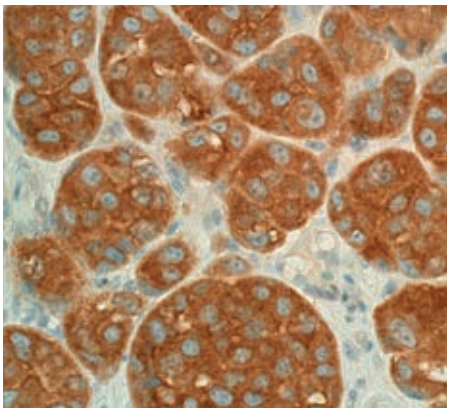


IMAGE: ORCHARD ET AL. (2019)

MICROBIOLOGY

Microbiologists will find interest in three papers. For virologists, toll-like receptors (TLRs) have roles in the innate immune system. Vidyant *et al*, from India and the USA, show, on pages 59-63, differences in an SNP in *TLR4* in 160 patients positive for HIV and 270 negative for HIV. However, this does not suggest that this SNP protects against HIV as the two groups may not have accrued the same risk factors for acqusition of the virus. Bacteriologists will find interest in two papers from Iran. Mahdavi and Isazedeh show, on pages 92-94, that *Lactobacillus casei* suppresses the expression of virulence-promoting gene *hfq*. This *in vitro* data supports the hypothesis of so-called "friendly" bacteria. Bakhti and colleagues report on pages 95-97 that *cagG*, but not *cagH*, *cagL* or *orf17* in *H. pylori* is more prevalent in duodenal ulceration than in gastric ulceration.

CPD

In common with previous articles, any of the above may be the subject of Journal-based learning. BMS

Andrew Blann is the Editor of the *British Journal of Biomedical Science*.

A rapid result is highly desirable so that, if needed, treatment can proceed as soon as possible

MY IBMS NEWS

AHAWARDS

IBMS MEMBERS WIN AWARD

IBMS members Claire Cameron, Sarah Smith and Lynne Taylor won the Scottish Government Award at the Advancing Healthcare Awards (AHAwards).

The AHAwards recognise the achievements and contributions of allied health professionals and healthcare scientists across the UK.

This year, the IBMS members, who are from NHS Lothian, won the Scottish Government Award for "driving improvement, delivering results" for their exceptional Science Training School.

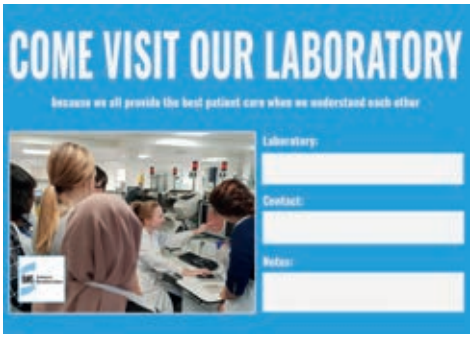
Sponsored by the Scottish Government, this award is for all healthcare scientists in Scotland who have demonstrated their expertise to drive improvement and maximise the contribution of healthcare science.

POSTER

Come Visit Our Laboratory

A new initiative called "Come Visit Our Laboratory" has been launched by the IBMS.

It features a poster for IBMS members to print, which was created by the IBMS and Sobana Qadus, a biomedical scientist at Manchester Foundation Trust.



The idea is to encourage other healthcare professionals to visit the laboratory and gain a better understanding of the job of biomedical scientists.

The poster says: "Come visit our laboratory because we all provide the best patient care when we understand each other."

Sobana said: "In healthcare, building effective communication and working practices can mean the difference between life and death. The best outcomes for patients are usually achieved when we all work together, learn together and progress our practices and services together."

The poster can be downloaded from the IBMS website and printed out in A4 or A3 and put up in staff rooms – encouraging people to get in touch and arrange laboratory tours.

→To download, visit bit.ly/BS_ComeVisit

NOTIFICATION

ANNUAL GENERAL MEETING

The seventy-seventh Annual General Meeting of the Institute of Biomedical Science will be held at the Institute of Biomedical Science, London, EC1R 5HL, on Saturday 8th June 2019 at 11.30 am.

Official notification of the meeting was published in last month's issue of *The Biomedical Scientist* (page 41) and was also featured on the IBMS website.

MEMBERSHIP BENEFITS

FREE LEGAL ADVICE FOR MEMBERS

One of the benefits of IBMS membership is access to its legal advice service at no extra cost.

The advice covers a wide range of topics, from unfair dismissal, redundancy and discrimination, through to motoring, personal injury and tax, among others.

The legal assistance helpline can be used to access expert advice any time of the day or night and all calls are totally confidential and free of charge.

The service is run by DAS UK Group, where enquiries are handled by teams of solicitors, qualified legal executives and law graduates.

Their legal services are designed to be appropriate for your needs, with advice that is as clear and jargon-free as possible. Their lawyers are skilled in customer care and providing sound legal guidance.

For law in Scotland or Northern Ireland, members will be referred to one of their specialist advisors, who are available 9am-5pm Monday to Friday (excluding public and bank holidays).

→ For more information, visit ibms.org/my-ibms/legal-assistance

GUIDANCE

UK SMI TP 34 and 38 reissued

The UK Standards for Microbiology Investigations (UK SMIS) has reissued guidance on X and V factor tests and thermonuclease tests.

Developed with the support of Public Health England working in partnership with the NHS and other professional organisations, UK SMIS has released the two documents pertaining to thermonuclease tests and X and V factor tests.

The guidance for UK SMI TP 34, for thermonuclease tests features updated references, subheadings to amend technical limitations, as well as information on the use of NCTC 6571.

The reissued guidance for UK SMI TP 38, relating to X and V factor tests includes updated documents, references and a flowchart to include commercial alternatives.

→ For more information, contact the Standards Unit, at the National Infection Service on standards@phe.gov.uk

IMAGES: ISTOCK

IBMS RESPONSE

ACADEMY FOR ADVANCING PRACTICE

The IBMS has responded to the Academy for Advancing Practice proposal by Health Education England (HEE).

It proposes to create an Academy for Advancing Practice and has drafted documents describing plans for its operation, standards for education and training and an equivalence route for recognition of advanced practice.

The IBMS said there does not appear to be a good general level of awareness of the plans for this academy and the consultation was only open for a very limited period of time.

The stated intention is to standardise routes into advanced clinical practice (ACP), recognise registered health and care practitioners who demonstrate the capabilities set out in the ACP or consultant practitioner framework, and take on responsibility for accrediting ACP education programmes.

While the IBMS does not wish to be negative of any measure that is intended to raise standards or provide a safer service for patients, it has raised a number of points, which are mainly based around a lack of clarity in the document.

In light of its concerns, the IBMS has recommended that the documentation is revised to more clearly define the role of the academy and the targeted levels of practitioner in the workforce, with clearer recognition of the differences of the different levels of posts and the qualifications required by healthcare employers.

→ To view the IBMS response, visit bit.ly/BS_response

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JOURNAL-BASED LEARNING EXERCISES

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

DEADLINE WEDNESDAY 4 SEPTEMBER 2019

The NHS Long Term Plan. Overview and Summary.

(Note: Questions are set on the overview and summary only, pp 1–10)
www.longtermplan.nhs.uk/wp-content/uploads/2019/01/nhs-long-term-plan.pdf
Assessment No: 060919

01	The NHS has been in operation since 1948.
02	Going forwards, there will be a provision of 2.2% funding increases annually.
03	The NHS is the largest employing organisation in the world.
04	There will be a major focus on digital systems going forwards, especially in primary and outpatient care.
05	The plan ensures that specific scientific and technical training programmes are developed to support the implementation of the plan.
06	The plan seeks to address health inequalities and demonstrate achievements via key metrics.
07	There will be a drive to expand treatment at home with more community health provision.
08	The plan will expand its mental focus to include autism and learning disabilities.
09	The plan acknowledges difficult-to-recruit specialisms and is looking at using new incentives in these areas.
10	The plan anticipates saving £70 million in five years.
11	The plan requires some changes to legislation.
12	The plan envisages the use of artificial intelligence.
13	There will be no extra funds available for CPD.
14	There will be a requirement for more-flexible rostering of workers.
15	The plan notes that research and development are critically important.
16	There is a commitment to reduce air pollution, smoking and obesity.
17	It is recognised that delays to hospital discharges will remain problematic.
18	Over three million people contributed individually to consultations on the plan.
19	The NHS has improved the outcomes for stroke and major traumas.
20	The plan notes that employees are under stress.

Eradication of measles: remaining challenges.

Holzmann H, Hengel H, Tenbusch M, Doerr HW. *Med Microbiol Immunol* 2016; **205** (3): 201–8. Assessment No: 060619

01	Measles virus (MeV) is commonly regarded as a bloodborne virus.
02	MeV can predispose people to opportunistic infections due to its impairment on memory B and T cells.
03	MeV is easily transmitted between humans and animals, and vice versa.
04	Twenty-four genotypes of MeV compiled in eight clades have been identified after sequencing the 450 nucleotides of the *N* gene.
05	The pathognomonic Koplik spots appear on the buccal mucosa at the start of the prodromal phase.
06	Subacute sclerosing panencephalitis (SSPE) is linked with MeV strains escaping specific immune responses persisting in neurons and glia cells of the brain.
07	The MeV reproductive rate is much higher in comparison to Ebola and influenza.
08	In the pre-vaccination era, MeV would be responsible for the deaths of 7–8 million children annually.
09	With the increased risk of exposure that an epidemic brings, MMR vaccinations can be recommended for infants as young as 6–9 months of age.
10	After vaccination programmes started in the 1980s, the incidence rate dropped by roughly 70%.
11	Most MeV strains start the infection process by the interaction of glycoprotein F to virus-specific cell receptors such as CD120.
12	Pregnant ladies who've previously had an MeV infection or vaccination have a level of immunity that can offer vertical protection to their infants.
13	Wars and the increased refugee migrations across Europe have increased the chances of the WHO reaching its eradication goal.
14	The low reproduction rate of measles means that you only need 40% of a population to be immune to ensure herd immunity.
15	Combined vaccines such as MMR lead to an impairment of the immunogenic infectivity of each of the single attenuated viruses.
16	For MeV surveillance systems to work appropriately within national health authorities, suspected cases must be reported rapidly.
17	On average, patients are at their most infectious six days onwards after the onset of exanthema.
18	Whilst being developed over 50 years ago, the Ender/Schwarz strains are still the preferred strains in the live-attenuated vaccine.
19	Within the laboratory, MeV diagnosis can be hampered due to false positives caused by recent vaccination history or cross-reactivity with other viruses.
20	The Rinderpest pandemic of 2010 has shown that *Morbillivirus* vaccines are ineffective.

REFLECTIVE LEARNING

01	What impacts and implications do you foresee for pathology services based on this plan?
02	How could point-of-care testing assist in early diagnosis and community care?

01	Apart from the viral vaccines mentioned in this article, there have been other vaccines available for use. Summarise a select few of these, including the challenges they have faced.
02	Reflect on the differences between innate and adaptive immune responses within the human body.

IBMS Institute of Biomedical Science
Continuing Professional Development

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

EVENTS AND TRAINING COURSES

DATE	TITLE	VENUE CONTACT
June		
5-6 Jun	**Clinical and Laboratory Haemostasis 2019; UK NEQAS for Blood Coagulation Annual Scientific Meeting**	Sheffield I tim.woods@sth.nhs.uk
6 Jun	**IBMS Registration Portfolio Workshop**	London I c.ferrier@westminster.ac.uk
6 Jun	**Update in Cervical Cytology for pathologists, consultant BMS and holders of the Advanced Specialist Diploma in Cytology**	Bristol I SWRCTC@nbt.nhs.uk
7 Jun	**UK NEQAS Roadshow**	Edinburgh I birminghamquality@uhb.nhs.uk
10 Jun-21 Jul	**Introductory Course in Cervical Cytology**	Bristol I SWRCTC@nbt.nhs.uk
11-12 Jun	**Practical and Clinical Microbiology of Anaerobes**	Cardiff I deborah_robinson@dwscientific.co.uk
12 Jun	**UK NEQAS Cellular Pathology Technique TEM workshop**	Leicester I chantell.hodgson@nhs.net
13 Jun	**Quality, Audit and Improvement workshop**	Croydon I sue.alexander@rmh.nhs.uk
13 Jun	**UK NEQAS Immunology, Immunochemistry & Allergy Quality Assurance Masterclass 19**	Sheffield I ukneqas@immqas.org.uk
13-14 Jun	**Anaerobe 2019: Changing perceptions of anaerobic bacteria; from pathogen to the normal microbiota and back; a Microbiology Society-focused meeting**	Cardiff I s.gavrila@microbiologysociety.org
14 Jun	**UK NEQAS Immunology, Immunochemistry & Allergy Annual Participants Meeting EQA 2019: Maximising Quality for Patient Care 19**	Sheffield I ukneqas@immqas.org.uk
19 Jun	**Employers Forum**	London I t.madgwick@westminster.ac.uk
19 Jun	**UK NEQAS Cellular Pathology Technique special staining beginners/refresher workshop**	Newcastle upon Tyne I chantell.hodgson@nhs.net
20 Jun-20 Jul	**UK NEQAS Cellular Pathology Technique specialist workshop A**	Newcastle upon Tyne I chantell.hodgson@nhs.net
25 Jun	**One-Day Update in Cervical Cytology – metaplasia/cancer audit day**	Bristol I SWRCTC@nbt.nhs.uk
July		
8-11 Jul	**Identification of pathogenic fungi**	Bristol I michael.palmer@phe.gov.uk
8-12 Jul	**Electron Microscopy Summer School**	Leeds I katejermey@rms.org.uk

DATE	TITLE	VENUE CONTACT
9 Jul	**Annual SHOT Symposium**	Harpenden I shot.symposium@nhsbt.nhs.uk
15-17 Jul	**Light Microscopy Summer School**	York I katejermey@rms.org.uk
15-26 Jul	**Introductory Course in Cervical Cytology**	Bristol I SWRCTC@nbt.nhs.uk
18-19 Jul	**Getting the most from your confocal course**	York I katejermey@rms.org.uk
26 Jul	**Train the Trainer**	London I c.ferrier@westminster.ac.uk
August		
7 Aug	**UK NEQAS Cellular Pathology Technique tissue preparation techniques workshop**	Gateshead I chantell.hodgson@nhs.net
8 Aug	**UK NEQAS Cellular Pathology Technique tissue morphology and recognition workshop**	Gateshead I chantell.hodgson@nhs.net
8 Aug	**UK NEQAS Cellular Pathology Technique non-gynae cytology beginners/refresher workshop**	Gateshead I chantell.hodgson@nhs.net
9 Aug	**UK NEQAS Cellular Pathology Technique non-gynae cytology intermediate workshop**	Gateshead I chantell.hodgson@nhs.net
14 Aug	**UK NEQAS Cellular Pathology Technique special staining beginners/refresher workshop**	Newcastle upon Tyne I chantell.hodgson@nhs.net
15 Aug	**UK NEQAS Cellular Pathology Technique specialist workshop B**	Newcastle upon Tyne I chantell.hodgson@nhs.net
20-22 Aug	**BSAC Residential Workshops for EUCAST Susceptibility Testing**	Cardiff I ecarruthers@bsac.org.uk
September		
4 Sep	**One-Day Update in Cervical Cytology**	Bristol I SWRCTC@nbt.nhs.uk
4 Sep	**UK NEQAS Cellular Pathology Technique immunocytochemistry staining beginners workshop**	Newcastle upon Tyne I chantell.hodgson@nhs.net
5 Sep	**UK NEQAS Cellular Pathology Technique immunocytochemistry intermediate/trouble shooting workshop**	Newcastle upon Tyne I chantell.hodgson@nhs.net
9-13 Sep	**Flow Cytometry course**	York I katejermey@rms.org.uk
11-12 Sep	**Beginners Immunohistochemistry**	Sheffield I l.baxter@sheffield.ac.uk
22-25 Sep	**IBMS Congress**	Birmingham I congress.ibms.org
October		
9 Oct	**Intermediate Immunohistochemistry**	Sheffield I l.baxter@sheffield.ac.uk
15 Oct	**UK NEQAS Cellular Pathology Technique Mohs workshop**	Gateshead I chantell.hodgson@nhs.net
16 Oct	**UK NEQAS Cellular Pathology Technique BMT workshop**	Gateshead I chantell.hodgson@nhs.net
17 Oct	**UK NEQAS Cellular Pathology Technique renal workshop**	Gateshead I chantell.hodgson@nhs.net
November		
11-12 Nov	**UK NEQAS CPT Annual Participants Meeting**	Dublin I chantell.hodgson@nhs.net
12 Nov	**Fine Needle Aspiration Cytology for Technical Staff**	Bristol I SWRCTC@nbt.nhs.uk
13 Nov	**UK NEQAS Cellular Pathology Technique non-gynae cytology beginners/refresher workshop**	Gateshead I chantell.hodgson@nhs.net
13-14 Nov	**Advanced Immunohistochemistry**	Sheffield I l.baxter@sheffield.ac.uk
14 Nov	**UK NEQAS Cellular Pathology Technique non-gynae cytology intermediate workshop**	Gateshead I chantell.hodgson@nhs.net
27 Nov	**UK NEQAS Cellular Pathology Technique TEM workshop two**	Leicester I chantell.hodgson@nhs.net
27 Nov	**Update in Cervical Cytology for pathologists, consultant BMS and holders of the Advanced Specialist Diploma in Cytology**	Bristol I SWRCTC@nbt.nhs.uk
December		
3 Dec	**One-Day Update in Cervical Cytology – HPV cancer audit day**	Bristol I SWRCTC@nbt.nhs.uk

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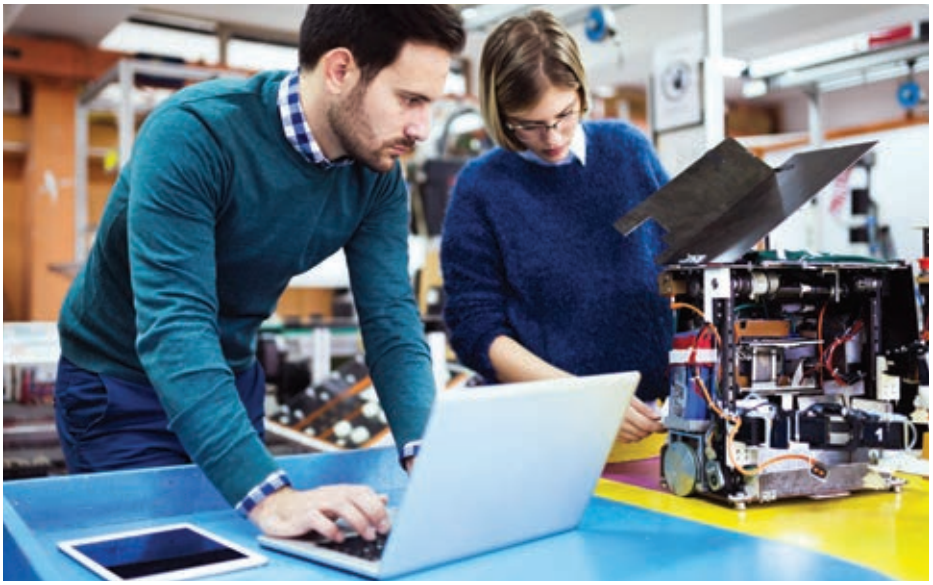
HERE TO HELP

JOURNEY TO THE INSTITUTE

Emma-Jane Plews has joined the IBMS in the role of Education Manager. Here she gives a short introduction of her path into the role.



I must begin by saying how great it has been to start at the IBMS, everybody has been so welcoming and I already feel like I have been here for years.

So, how did I end up here? I didn't have a great deal of knowledge of biomedical science in my younger years, until I began working within the blood sciences department at my local hospital. It was here that I learnt the basics of a clinical laboratory, which ignited my interest in biomedical science. It was also here that I discovered histopathology down the corridor and decided this was the path I wanted to explore further. I enrolled onto an Access to Higher Education course and the following year I progressed on to study biomedical science at the University of Kent, accredited by the IBMS, of course.

I worked and studied for four years whilst bringing up my two small children. It was a particularly challenging time for me but with fantastic support (thanks mum!) I made it through and graduated with a BSc (Hons) and a new job in histopathology. Over the following two years I built up my knowledge and experience and I became registered with the Health and Care Professions Council as a biomedical scientist, having achieved the IBMS Certificate of Competence. Following my registration, my passion and experience grew and I became the lead for special stains, which is still my favourite area of histopathology.

During my time working within histopathology, I was also extremely fortunate to take part in a few Science, Technology, Engineering and Maths (STEM) events, promoting biomedical science to secondary school students. This prompted the beginning of a change, as I realised that not only did I have a passion for biomedical science; I loved promoting and teaching people about it too. This led me into the role of Healthcare Science Assessor, where I undertook the Teaching, Assessment and Quality Assurance award to become a qualified assessor. Although it meant leaving behind histopathology, I was very excited to become involved with the training and development of biomedical science support staff, who I hope may progress to become biomedical scientists in the future. This was a demanding but very rewarding role which allowed me to gain a deeper understanding of training and the needs of the candidates undertaking qualifications within the laboratory.

From there, I came across this opportunity to become part of the education team at the Institute. I believe my skills and experience will enable me to help and support members allowing me to excel within this role. Over the coming months, I am looking forward to developing further and help promote excellence within biomedical science.

IMAGES: ISTOCK

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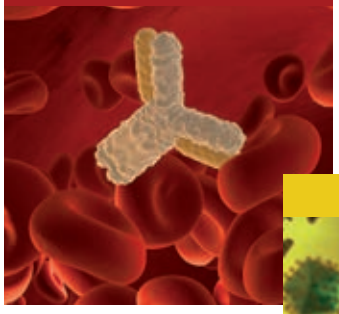
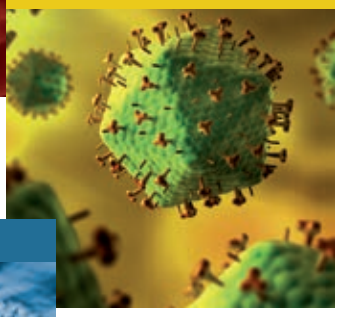
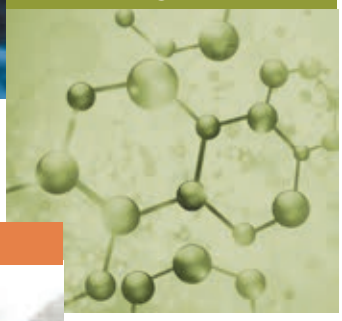


Infectious Serology



Allergology

Antigen Detection



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For further details on either role listed above, contact Kelly Thwaite via email: **kelly.thwaite@tdlpathology.com** or visit the TDL website for a full list of roles available across the company: **www.tdlpathology.com**.

Closing Deadline: Friday 14th June 2019

Chief Biomedical Scientist (deputy laboratory manager)

NHS Hull University Teaching Hospitals NHS Trust

Applicants are invited for the post of Chief Biomedical Scientist (deputy laboratory manager) in the Microbiology laboratory at Hull University Teaching Hospitals NHS trust.

This exciting opportunity will see the successful applicant joining a dynamic laboratory team which is part of a wider Infection Department. The laboratory team works closely with the Infection clinicians to provide a high quality diagnostic service to the Trust and local community services. This innovative department is committed to improving patient care and the Trust Pathology Quality team was the winner of the International Quality Award 2018.

The wide variety of work and expertise available at Hull Royal Infirmary and Castle Hill Hospital (virology department) provides an ideal environment for a Chief Biomedical Scientist to develop. The department has a wide test repertoire and the latest in molecular equipment. This is a challenging post for an enthusiastic, well-motivated, forward thinking individual who will be expected to make a significant contribution to the development of the department. The successful applicant will be a qualified BMS, with MSc, or equivalent, will be responsible for the day-to-day operational running of the Microbiology department. Applicants must be state registered with the HCPC and have extensive post registration experience in Microbiology (see JD).The post holder is the manager responsible for the day to day delivery of a medical laboratory service that achieves the objectives of efficient and effective patient care. He/she is directly responsible to the Laboratory Manager for the quality management in accordance with departmental and Trust policies and procedures, and is the departmental quality link for microbiology and virology.

Informal visits to the department are encouraged.

** Salary relates to year 1 of 3 year NHS pay deal, year 2 available from April 1st 2019

For further details of the post please contact Alison Eyre Laboratory manager Microbiology 01482 816779 alison.eyre@hey.nhs.uk

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Applicants should be driven and passionate with good interpersonal abilities who wish to evolve their existing skill-set within a supportive environment. We would also be interested to hear from Biomedical Scientists (Band 5) who have at least 12 months experience and who are due to complete their IBMS Specialist Portfolio within 6 months.

ABOUT US

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The following posts have been created to support the introduction of additional work and new technologies into the site. This is an exciting period of evolution and the successful applicants will be key members of the department, contributing significantly to the provision of the clinical diagnostic service and its development.

TDL are rightly proud of the excellent working environment that has been created at the Northwick Park Hospital laboratories. As well as a competitive, NHS reflected salary package, staff can expect a varied CPD programme led by our Education and Training Faculty, equipping them for a rewarding and accomplished career.

Deputy Head of Biochemistry *(ref: NWPDH3460)*
Service Lead for Microbiology *(ref: NWPMI3002)*
Senior Biomedical Scientist - Microbiology *(ref: NWPMI3041)*
Biomedical Scientist - Microbiology *(ref: NWPMI2969)*
Biomedical Scientist (Night Shift) - Microbiology *(ref: NWPMI3149)*
Biomedical Scientist - Haematology *(ref: NWPHM3357)*

For further information on the roles listed above, email TDL quoting the reference number: **jobs@tdlpathology.com**.

Closing Date: **16th June 2019**

The closing date may be earlier where there is high interest.

TDL is a committed equal opportunities employer and does not unlawfully discriminate on the basis of any status or condition protected by applicable UK employment law.

MY LAB

ROTHERHAM BIOCHEMISTRY DEPARTMENT

Senior Biomedical Scientist and Pathology Research Coordinator **Holly Neill** gives a guided tour of her laboratory.

The biochemistry laboratory at The Rotherham NHS Foundation Trust (TRFT) is part of the joint pathology partnership with Barnsley Hospital NHS Foundation Trust – Barnsley and Rotherham Integrated Laboratory Services (BRILS). As a combined pathology service, we serve a population of over 500,000 across both Barnsley and Rotherham.

At Rotherham we are a fairly small team that provides services predominantly to hospital patients, as well as some specialist referral work from other laboratories across the country. We work together with haematology and immunology to form a blood sciences department, analysing approximately 2000 samples per day across all disciplines. Our hard-working teams across blood sciences range from consultants and biomedical scientists, to medical laboratory assistants and clerical staff; all have a vital role in the smooth running of the laboratory and aim to provide a high-quality service.

The biochemistry department has two main sections: automation and specialist chemistry. The automation section is where the bulk of our work goes, analysing various samples from around the hospital on our automated chemistry and immunoassay analysers, 24 hours a day, seven days a week.

Much of our urgent work comes from our newly built Urgent and Emergency Care Centre, which provides a number of services to ensure patients access the most appropriate treatment. We have just introduced a new high-sensitivity troponin-I assay, which aims to increase patient discharge safely from A&E, as well as decrease admissions and the amount of time patients spend in hospital waiting on serial results. Our new pathway can admit or discharge on the first sample and a second sample can be taken at one hour, if required, instead of six. This allows for more timely patient management and care. We also process routine work from other wards and small amounts of GP work, the bulk of which goes to Barnsley Hospital.

Our specialist chemistry section uses HPLC to measure vitamins A, E, B1 B_6 and C by UV and fluorometric detection, as well as electrochemical detection for catecholamines, metanephrines, VMA and 5HIAA analysis in urine. Staff rotate through both sections and the immunology department, providing them with a range of practical and analytical skills as well as developing their knowledge in different areas.

The biochemistry laboratory at TRFT has worked hard to become fully UKAS ISO:15189 accredited, with our first surveillance visit this January.

We are accredited for Registration and Specialist Portfolio training and have several people undergoing their IBMS Specialist Portfolios and a student from Sheffield Hallam University starting with us in September to complete their IBMS Registration Portfolio. We believe that investing the time in staff and students not only helps them to grow and develop in the laboratory, but will also encourage them to stay within the profession and be enthusiastic about their job. We are also passionate about CPD and have monthly tutorials and "Cases and Cakes", where we discuss interesting cases and get to eat some cake over lunch time.

Our hope for the future is to continue to develop and improve our service by recruiting more staff, investing in innovative new technology and promoting the vital work that all pathology laboratories provide in order to deliver the best patient care to the communities in our area.

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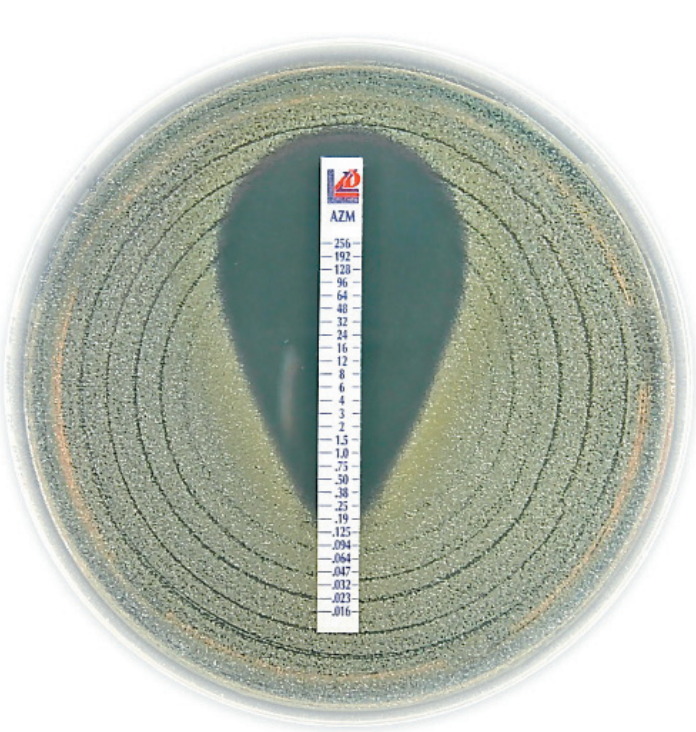

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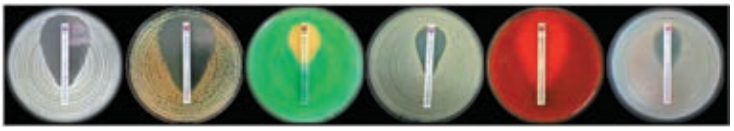

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