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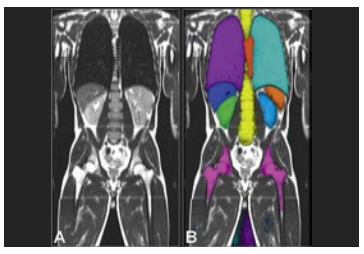

No change: NHS is still vulnerable to cyber attack

John Lockley MD, a former general practitioner (GP) and committee member of the SystmOne National User Group (SNUG), is a NHS IT analyst and commentator on cyber security.

The recent global WannaCry ransomware cyberattack had a particularly acute impact on health services across the United Kingdom, leaving the country's National Health Service (NHS) vulnerable to cyberattack, Mark Nicholls reports

While affecting computers across the world – including Russia, EU countries and the USA –the United Kingdom's NHS hospitals were forced to cancel routine surgery and GP appointments as systems were affected by the recent global cyberattack, or were proactively shut down in an attempt to avoid the infection.

Some hospitals diverted patients away from their accident and emergency (A&E) departments, while large amounts of electronic patient data became unavailable.

As the inquest opened on why the NHS was so easily hacked, the initial focus fell on out-dated computer systems and unsupported software – notably Windows XP – which is still in widespread use in the NHS, and whether software patches issued by Microsoft to offer protection to current Windows software had been installed.

Bugs in the healthcare IT system - no medical answer against them

Hospitals in England and Wales hit, but not others

In England, 47 NHS trusts reported problems at hospitals and 13 in Scotland, while services in Wales and Northern Ireland were seemingly unaffected.

England's biggest NHS trust, Barts Health NHS Trust, which runs five hospitals in London, was forced to reduce surgery and cancel outpatient appointments.

Whilst it emerged that Microsoft identified a risk in March and sent out patches, some trusts might have delayed installing them.

Various criticisms about the quality of IT security in the NHS have been made in recent years with a number of high-level warnings.

The Care Quality Commission and National Data Guardian, Dame Fiona Caldicott, wrote to health secretary Jeremy Hunt last summer warning that an 'external cyber threat is becoming a bigger consideration' within the NHS.

The NHS continues to face financial constraints amid suggestions that funding had been diverted away from cyber security, but the government has rejected this, saying the NHS had upgraded its security before the incident, with £50 million made available to further improve security.

The WannaCry ransomware behind the latest cyberattack locks many types of users' files and demands a $300 (£230/270 Euros) payment to allow access. Although the indications are that the main repositories of patient data were not directly affected, access to ancillary was locked, effectively choking the daily operating patterns of the NHS.

Meanwhile, Chris Hopson, chief executive of NHS Providers, said many hospitals use sophisticated technology such as MRI and CT scanners which are 'bound to be using old software' because they have a 10-year life expectancy and, consequently, often use older operating systems.

NHS IT analyst and cyber security commentator Dr John Lockley remains concerned that the NHS has not had a consistent and country-wide approach to cybersecurity for a number of years and so continues to leave itself vulnerable to attack. Since the demise of NHS National Programme for IT there is no longer a centralised approach to updates, with each trust independently responsible for its actions.

Too slow a response to migration from XP to later Windows version

However, the recently-developed NHS Care Computer Emergency Response Team (CareCERT) offers advice and guidance to support health and social care organisations in responding effectively to cybersecurity threats.

Dr Lockley remains concerned that the risk of cyber attack within the NHS remains high, for a number of reasons. First, he says, the NHS has had an extremely slow, uncoordinated response to migrating away from XP to the more secure and patchable later versions of Windows. Second, despite Microsoft making critical patches for these later programs in March, many trusts have not installed them, adding that there is, as yet, no robust national mechanism for policing the installation of upgrades.

Whilst acknowledging that certain types of medical equipment and programs still need XP because they would not be compatible with later systems, he adds: 'Unless you disconnect all vulnerable computers from the outside world – physically or with special software techniques – they will always remain a risk to the safety of systems and networks.

'If you have a weak point, you either have to protect fully against the possibility of anybody getting in, or not use those computers.' The key to adequately protecting the NHS against further cyberattack, he concluded, is to instigate a robust, fully-funded and policed nationwide programme to replace XP and other legacy software across the entire NHS.

Additionally, key steps are to

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House of Lords wants a new Office for Health and Care Sustainability

Short-sighted politicians place NHS in jeopardy

Report: Mark Nicholls

The future of the National Health Service is under threat unless action is taken to address critical issues, according to members of the UK's House of Lords. In a hard-hitting report, the House of Lords Select Committee on the Long-Term Sustainability of the NHS criticised the 'short-sightedness' of successive governments for failing to plan effectively for the long-term future of the health service and adult social care.

With longer waiting lists for patients and funding shortfalls, a recent survey suggested that 55% of people in the UK also fear the NHS will deteriorate further at a time when there remains uncertainty over the impact the UK's decision to leave the EU on attracting people from other European countries to work in the NHS.

Tax-funded free at the point of care still the most effective way to deliver care

In its report, the Committee stressed that the UK system of a tax-funded, free-at-the-point-of-use National Health Service remains the most efficient way of delivering healthcare, now and in the future.

However, for that principle to remain, members stressed that many aspects of the way the NHS delivers healthcare will have to change. Suggesting that a 'culture of short-termism' exists within health and social care provision in the UK, the Lords recommend that a new, independent, Office for Health and Care Sustainability should be established to look at health and care needs for the next 15-20 years.

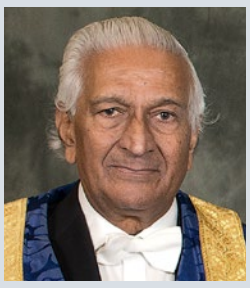
The office should report to Parliament on the impact of changing demographic needs, the workforce and skills mix in the National Health Service and on health and social care funding.

With a merging of health and social care in the UK, the Lords Committee expressed concern that funding between the two has been poorly co-ordinated. The report says that the failure to implement a long-term strategy to secure a skilled, well-trained and committed workforce that the health and care system will need is, the 'biggest internal threat to the sustainability of the NHS.' It also advocates a reshaping of primary and secondary care, and specialised services, and pointed out that service transformation is 'at the heart of securing the long-term future of the health and care systems.'

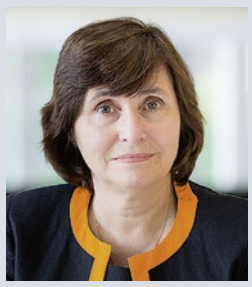
Among the 34 recommendations the committee makes are for budgetary responsibility for adult social care at a national level to be transferred to a new Department of Health and Care; NHS England to engage with general practitioners (GPs) to examine alternative models; NHS England and NHS improvement to be merged to create a new body with simplified regulatory functions; the Government to commission an independent review to examine the impact of pay on morale and retention of health and care staff; national and local public health budgets to be ring-fenced for at least the next ten years; a nationwide campaign to highlight the dangers of obesity; the NHS Constitution to be redrafted to emphasise that access to the NHS involves patient responsibilities as well as patient rights.

A shocking lack of long-term strategic planning, says Peer of the Realm

'The Department of Health at both the political and official level is failing to think beyond the next few years,' confirmed Lord Patel, committee chairman and eminent obstetrician. 'There is a shocking lack of long-term strategic planning in the NHS. To solve this we need a new body that is independent of government and is able to identify clearly the healthcare needs of a changing and ageing population and the staffing and funding the NHS will require to meet those needs.'



Lord Patel KT – Narendra Babubhai Patel – is a renowned British obstetrician, cross bench peer, and Chancellor of the University of Dundee. He has served as Vice-President of the All-Party Parliamentary Group on Maternity Services since 2002 and in the group on Infertility Services since 2003. He is also Chairman of the Stem Cell Steering Committee since 2003 and a member of the Science and Technology committee.



Professor Jane Dacre was elected President of the Royal College of Physicians (RCP) in April 2014 and is an honorary consultant physician and rheumatologist at the Whittington Hospital in north London, professor of medical education, and director of UCL Medical School in London.

15-20-year plans, but NHS will also need bigger funds especially for low paid

He emphasised the need to look ahead and plan for 15-20 years into the future. 'We also need to recognise the NHS will need more money. NHS spending will need to rise at least as fast as GDP for 10 years after 2020,' he added. 'One area where more spending will be required is on pay for lower paid staff.' Commenting on the House of Lords Select Committee report, the Royal College of Physicians (RCP) President Jane Dacre welcomed the report's focus on transformation and the call for a long-term strategy on caring for a changing population. 'If we are to improve the care for patients we treat, as clinicians, in collaboration with patients, we need to reshape the secondary and specialist care we provide.'

Danny Mortimer, chief executive of NHS Employers, said: 'It's imperative the health and social care sector is able to attract and recruit the right staff in order to protect its future, whether that be from the UK or abroad. 'We also agree that there is a need to give assurances to EU nationals, who make up 6% of the health and care workforce, that they will be able to remain, as well as encouraging them to do so.'

Across the UK, the NHS is currently struggling to cope with patient demand. Funding is rising – an extra £8 billion has been made available by the present conservative government – but this still does not appear enough to cope in a health system that sees a million patients every day and employs 1.7 million personnel (making this the world's fifth biggest employer).

However, despite the issues, the NHS continues to be innovative, leads ground-breaking research and conducts millions of successful – often life-saving – treatments.

Last year saw £140 billion spent on health across the United Kingdom, yet patients at present are waiting longer to see their GP, or for a hospital appointment, for surgery, or to be seen in the Accident & Emergency (A&E) department. A key target stating that 95% of patients arriving at the emergency department should be seen within four hours has not been achieved for two years.

However, the number of people visiting A&E have risen by a third in 12 years.

Hospitals and health services across the UK are also facing austerity measures and being asked to make savings to balance budgets, often meaning that the criteria for offering routine operations, such a hip replacements or cataract surgery, is being changed with patients having to wait longer, or until their condition has deteriorated further, before surgery is offered.

Health and social care services in the UK are faced with an ageing population; people living longer with chronic conditions; an obesity crisis and rising drug costs.

That is combined with difficulties in filling nursing or GP posts, despite the creation of more training positions, and an emphasis towards greater community care but with an infrastructure still centred on a network of district general hospitals.

Danny Mortimer became Chief Executive of NHS Employers in November 2014. His first work in healthcare was as a porter and care assistant before he became a management trainee. He later held a series of director and executive roles before joining NHS Employers, the voice of employers across the English NHS. He also chairs the Cavendish Coalition of social care and health organisations.

Plan to draw hospitals and local community teams closer together

NHS England chief executive Simon Stevens has set out a five-year plan to create more integrated care, which involves hospital services working more closely with their local community teams.

However, there remains an imbalance in health and social care funding with significantly more money still spent on front-line healthcare than social care.

No chance: Still vulnerable to cyber attack

Continued from page 1

methodically and routinely apply patches and upgrades; use antivirus software and keep it updated; back up data files regularly and frequently; and teach staff to check the veracity of attachments and links in emails they receive, because this is often the route through which ransomware first infects an organisation's computers.

AXREM - the trade association representing suppliers of diagnostic medical imaging, radiotherapy, healthcare IT and care equipment in the UK – warned that, while patches were available for medical imaging systems, robust network defences are critical in preventing future attacks.

While suppliers have been focusing on restoring operation of systems compromised by the Ransomware attack, and protecting systems from further risk, AXREM pointed out that, as medical imaging systems are classified as medical devices and subject to strict regulation, suppliers are obliged to rigorously test software updates and patches to ensure that functionality and safety is not compromised.

The organisation warned that 'for this reason, the reliance upon provision of clinical product software patches for defending against malware attacks does not provide a sustainable option', and stressed: 'therefore, robust network defences are strongly recommended to prevent against future attacks'.

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Family d the alar

Report: Madeleine van de Wouw

Three quarters of Dutch general practitioners (GPs: family doctors) experience an increasing work pressure, according to a recent survey of the National Association of General Practitioners (LHV). Especially evening, night and weekend services at GP Emergency Posts (Dutch: HAP) are found to be heavy duty, in addition to their daily practice.

Too big a success

Established some 15 years ago to relieve individual service pressure on GPs and to improve healthcare, the HAPs (which are not Hospital Emergency Posts) soon became too big a success. Initially intended for patients needing urgent care, they HAPs are increasingly used by patients who either don't have a personal family doctor, or by those who actually don't have urgent medical issues. This puts at risk patients who do need immediate care, because they might have to wait longer. It also increases healthcare costs and, to make enlarge the problem, work pressure has increased rather than decreased. The HAP, in itself, has become an emergency.

Different questions

Besides the extra HAP work, population aging, increasing psychological complaints, refugees influx, decentralisation of youth care and on-going care for chronic patients are factors in increasing work pressure.

'People are becoming increasingly concerned with health and want to resolve issues and complaints immediately,' observes Andy Kwee (50), an independent GP in Almelo, with a medium-size practice (approximately 2,200 patients). 'The most important task of a GP was to make a diagnosis. Nowadays patients check their medical complaints on the Internet and find the most terrible diseases. As family doctors it's our job to reassure the patient, make him or her feel comfortable again and after that try to diagnose. Given all of that, the ten minutes we have for a consultation are not nearly long enough.'

Administrative hassle

In addition to all this the GP received additional duties. For instance taking over certain forms of hospital care, such as monitoring diabetes patients. 'And,' Kwee points out, 'there are so many forms and papers you have to fill in for healthcare providers, the government and health insurers. Then, I don't even count the individual requests by patients who need a letter from me for some reason or other. Compared to 2015, the costs of staff in 2016 increased by 40 percent because I employed more assistants to take over some of my work. Our public health minister may emphasise that the pressure and the administrative hassle are not too bad, but unfortunately she's wrong about that.'

This is confirmed by the LHV: 'When choosing the policy to organise more care in the first line, the

verworked Dutch physicians protest against hefty responsibilities

doctors sound m

Andy Kwee MD is a general practitioner in a medium-size practice in Almelo, the Netherlands. He is responsible for the care of approximately 2,200 patients annually and currently finds the government increasingly piling bureaucracy onto his heavy workload.

increased workload experienced by GPs was not well estimated in advance.'

Free days are not really free

GPs therefore go overboard to give their patients the quality of care and attention they would like to provide. 'I'm still doing my job,' Kwee emphasises, 'but we're stretched to the limit with all those extra tasks.'

Therefore, Kwee uses his scarce days off to manage administrative duties, and sometimes also patients. 'Recently I had a patient requesting euthanasia. It's impossible to give patients like this the time they need on a regular workday. You have to assist for at least for a couple of hours. So I went to see him and help him on my day off. I want give every patient of mine the care he deserves and needs.'

Plans for the future

The LHV survey is a first step in a larger plan to future-proof evening, night and day care where, in addition to GPs, also patient organisations, health insurers and the government are involved. For example, LHV is in consultation with the Ministry of VWS to invest part of the 2018 budget for more time for the patient, which is what doctors need: time; not only to invest in patients, but also in their practice. More doctors, more support staff.

But, the future looks grim: the government wants to remove even more duties from medical specialists and hand them over to the GP because they receive a lower rate. This plan is really not executable with the average number of 2,200 patients per practice, the LHV believes. To achieve this, practices must be reduced to up to 1,800 patients; otherwise GPs will be even more overloaded. A side effect of this is that, because of GP shortages, more people will visit the HAP. It's almost a vicious circle, which increases the risk of a burnout even more.

Prevention of long-term stress and a good demarcation of the task package and workload are therefore important tasks for professional organisations (LHV, NHG, KNMG).

What to do

Possible solutions are adjustments in the GPs protocol. The Dutch GPs established this, but it proved to be not strict enough. Additionally, the splitting of services, triage by a GP, or task recruitment, and a shift in the division of work between HAP, ER and RAV (Ambulances) at night presents a great deal to win. Pilots will begin for these solutions before summer, with first results expected in autumn.

Reducing administrative burdens is also important: fewer forms, fewer requirements. Both doctors and health insurers will benefit from that.

Doctors everywhere suffer the same stressful pressure

Andy Kwee 'There's no difference in being a family doctor in a village or city,' Kwee points out. 'Everyone has to deal with increased stress and work pressure. Fortunately, I still love my job. My first priority is to provide good care to my patients, and I hope to be able to do so for a long time.'

Software offers specifically designed deep learning algorithms

AI develops beyond the breast

Access, accuracy and efficiency are at the core of Samsung's healthcare strategy, explained Insuk Song, Vice President of Product Planning, Healthcare and Medical Equipment at Samsung Electronics, during our exclusive European Hospital interview. Samsung, the Korean giant, is now proceding with its artificial intelligence (AI) deployment, notably with the S-Detect software to help ultrasound professionals detect and characterise lesions in breast cancer.

Interview: Mélisande Rouger and Daniela Zimmerman

EH: Samsung is present in many industries. How does that experience translate into healthcare?

Insuk Song: 'We bring technological excellence from the electronics segment, which has strong synergies with healthcare. One is definitely imaging excellence. We are the leading provider of TV, with latest display technology such as the QLED TV. Many of our engineers come from the visual display background. Image processing and how to generate the best image is in our DNA.

'We are also very experienced in thinking of customer needs in terms of design and user experience. We are regularly awarded for our work in electronics design, and, earlier this year, three of our ultrasound products and one digital X-ray received the iF design award.

'Patients still need to adopt very difficult postures for medical imaging examinations, so we see that as an opportunity to innovate and accelerate innovations in an industry long dominated by a few key players. We are working on efficiency of workflow and ergonomic measures. Expediting workflow while easing ergonomic pain is a consideration for patients. If they're comfortable, you can scan them much easier, so it's win-win for them and the hospital.'

What distinguishes Samsung in the healthcare market?

'Mobility is our strong suit. Access is an issue: population is ageing and access to the hospital is sometimes a challenge, so making things small and accessible for patients anywhere is essential. In hospital a lot of patients are also immobile. Our mobile digital X-ray GM85 is one of the smallest and lightest in the world, and can go anywhere in the hospital. We will present our updated mobile fleet, at the upcoming RSNA.

'Diagnostic accuracy is fundamental to this industry. Good image quality is a base, but we are adding additional software capability to enhance the diagnostic capability of the radiologist or clinician, by enabling them to see beyond their own eyesight.'

How are your research projects in AI and deep learning tools advancing?

'We started working in that field a long time ago! We launched AI tools for breast cancer (BC) diagnosis – but nobody listened then. There was a lot of mental resistance and regulatory bodies are always very careful when a new diagnostic product arises.

'Our S-Detect software, which uses specifically designed deep learning algorithms, is a great tool to help radiologists diagnose BC. They don't need extra help for cases that are black and white; but they may do for tricky cases. Even experienced professionals are sometimes faced with challenging cases. What we claim is that we're their second opinion, we're here to help them double check. This software is not just run on our own brain, it is based on the experience of many radiologists. So you run S-Detect to see what other people might think of the tricky case at hand.

'AI is now a trend and it's easier to work in that area. We're trying to expand the capability of computer-aided diagnostic software in ultrasound and digital X-ray. We will also see chances of expanding it to other modalities and to other organs. S-Detect started in the breast, but it has already expanded to the thyroid and we're looking at other potential targets, the liver, for example.

'Whilst we receive a lot of support from this trend, it has raised the bar for regulatory bodies, which will now probably make a new regulation to ensure patient safety.'

You have international branches. Where do you encounter the most difficulties?

'Every market has its own challenges. For example, Europe is difficult because it has different languages and cultures. Although we treat Europe as Europe, there are many countries with different governments and regulations, so you need multiple strategies to obtain the same result.

'In the case of the United States, things are also very different from one state to another. Every customer is different in his or her own way. Although they buy the same machine, customers have their own requirements in terms of image quality. One setting will be fine for some but not for others.'

Can you learn from TV or mobile technology customers?

'Samsung Electronics operates in most countries, so we leverage with every culture and understand basic market culture. But healthcare is different. Although you know the TV market very well, that does not mean you know hospital markets. For healthcare you need to acquire additional capabilities that are very specific to this industry.

'We see the synergy with mobile technology at some point. With the challenges in healthcare systems today there are increasing needs to integrate patient care in the hospital as well as home, and we know it could be a great asset for us to offer that within the same product.'

Insuk Song PhD took on the role of Vice President and Product Planning Team Leader at Samsung Electronics in 2016. Prior to this she was the firm's VP of HME Marketing and, from 2009-2014, Senior Director of APAC Sales & Marketing for GE Healthcare, following her employment as Senior Consultant for the MacKinsey&Company (2001- 2009).

Tens of thousands of refugees arrived in Munich

'We saw unimaginable medical conditions'

In a vulnerable system the most vulnerable users suffer most – and in the German hospital surgical care system the most vulnerable are children – and, above all, immigrant children.

Quite a bit of whingeing was heard at the 134th German Surgery Congress in Munich regarding the inadequate framework conditions to provide safe and reliable surgical services in hospitals and private practices: not enough staff, too much bureaucracy, the commodification of healthcare.

But, there were also encouraging news, surprisingly in the context of demographic change. Demographic change is not only about an ageing population, it is also about the growing number of children due to increasing birth rates in Germany and the influx of immigrant children and adolescents. Their care is a particular challenge to the healthcare system, not only in financial terms but also right upon hospital admission.

Munich medics beat a huge challenge

In summer 2015, Munich showed true grit when tens of thousands of refugees, many of them children and teens, arrived in the city after a gruelling journey in the sweltering heat and had to be provided with medical care right in the reception camp. 'Among the refugees we saw unimaginable medical conditions,' reports Professor Stuart Hosie, Medical Director of the Department of Paediatric Surgery at Klinikum Schwabing, still visibly shocked. 'We saw a kidney tumour that covered the entire abdomen. We saw families who carried their children, paraplegic after a war injury, all the way to Germany. Not to mention the TBC cases in numbers that were to be expected.' It was a state of emergency in all hospitals throughout Munich but, looking back, the paediatric surgeon is proud to say 'the hospitals took on and mastered the enormous challenge of caring for the refugee children'.

It was a steep learning curve for everybody involved. One major take-home lesson: without volunteers the feat would not have been possible. In the reception camp Bayernkaserne in Munich three volunteer paediatricians had a first look at the children so they could be sent on to the hospital in the Munich centre in an orderly fashion.

There, samples were taken to test for multi-resistant bacteria. According to Hosie unaccompanied adolescents were a difficult group as many of them refused to stay in the hospitals, while others were grateful for the help they received and enjoyed the 'luxurious' hospital care.

Hospital staff as interpreters

Immigrant children who need medical care and their families are under extreme stress and the difficult overall situation is exacerbated by language and communication problems.

Hosie: 'We were lucky to be able to draw upon our pool of foreign staff.' More than 100 employees with basic clinical or nursing training and mostly native speakers of 35 foreign languages offer interpreting help in all sites of the Munich Municipal Hospital Group.

75 percent of the internal interpreters have a nursing background. The internal interpreting service not only supports the hospital staff with diagnoses and medical reports and information sessions, but is also available free of charge for patients and their families.

Foreign patients, however, who are scheduled for treatment, have to pay the interpreting service and most patients from Arab countries bring along their own interpreters.

Intercultural care is a major and important task for the hospital: Of the German cities with more than 200,000 inhabitants, Munich has the second largest percentage of foreigners (23.0 percent) with Frankfurt holding the top spot (25.9 percent).

Serving approximately 1,000 non-German patients per month, the Munich Municipal Hospital Group is assumed to be the largest provider of in-patient services for immigrants.

The group's department for intercultural care wants to dismantle linguistic and cultural access barriers, increase intercultural competency in the care of non-German patients and develop a service offering geared towards immigrants.

The experienced nurse often observes more

A brochure, published by the Federal Government's Commissioner for Migrants, Refugees and Integration, on the particular needs of immigrant patients supports the efforts. Paediatric surgeon Hosie points out that today all major paediatric clinics in the larger cities are well prepared to meet these needs.

However, children require adequate care across all clinical disciplines and there is a marked lack of comprehensive paediatric centres providing child-oriented environments that are suited for teaching. The crucial issue, however, is the shortage of paediatric nurses since the number of nurses correlates with mortality, no matter the country of origin of the young patients. As Hosie underlines, 'an experienced nurse sees more that an inexperienced physician'

Following studies at the University Nueva Granada, **Professor Stuart Hosie** received his medical training at the Military Academy and Central Military Hospital in Santa Fé de Bogotá in Columbia (1981 to 1987). He his interest in paediatric surgery began in 1988, at University Hospital Eppendorf, Hamburg, Germany. In 1991, based in Düsseldorf, he became licenced to practice in Germany. Via Mannheim, Hosie went to Heidelberg, completing his habilitation there in 2003. In 2006 he was appointed Professor for Paediatric Surgery at Technical University Munich. He is also Medical Director of the Clinic of Paediatric Surgery at Schwabing Hospital, a facility of the Munich Municipal Hospital Group. The professor is also a member of the board of the German Society for Paediatric Surgery (DGKCH).

Spanish hospital bets on artificial intelligence to improve results

'Radiologists are about to disappear'

San Carlos Hospital in Madrid has undertaken a number of projects to promote artificial intelligence (AI) use in clinical practice. Dr Julio Mayol, Medical Director and Head of the Innovation Unit, explained these initiatives and the direction he wants to take in an exclusive interview with European Hospital Correspondent Mélisande Rouger

'We are developing AI solutions to manage mental diseases and computational systems to help in clinical decision-making in situations such as mental disorders or hyponatremia, a condition in which patients present with low levels of sodium in their blood,' explained Julio Mayal MD, Medical Director of the Innovation Unit at San Carlos Hospital in Madrid.

'We have a partnership with Fujitsu for an AI apps project, which is a very large part of our work. AI helps us manage patients, and predict and improve patient outcome. For the moment we are developing tools for patients inside the hospital, but our goal is to expand to outpatient care.

'We are also working with Touch Surgery on a simulation app for our surgery students, available on both smart phones and tablets. It's in the early stage, so I can't really give more details, but it's a very interesting process because it helps us capture data on how human beings think when they must resolve a problem.'

Why are you betting on artificial intelligence?

'We want to change healthcare. Society is continuously evolving and we need to be in the driving seat to try and accelerate changes as fast and appropriately as possible. I believe AI and technology enabling data analysis are essential in a world depending on and generating so much data.

'Besides, it's important to be able to evaluate, to measure what we are doing. This is a global trend in medicine, which we follow at San Carlos Hospital. We aim to improve our results for patients, not increasing our service production. We already offer a lot of services; now we need to know what we obtain exactly. Right now, we don't know that. We don't know precisely how a patient is doing after one or five years of surgery, for instance. This is the kind of information we really need to have right now.'

Will artificial intelligence replace some medical disciplines?

'Every discipline relying and depending on images are at risk of disappearing. Radiologists are about to disappear. Technology is going to replace them because machines will read studies far better and more precisely than humans ever could. Anatomy pathologists are next in line.

'Many people don't see they are in danger; actually most human beings don't see the danger they are facing. Those who don't understand they need to adapt are the most at risk.'

Other hospitals in Spain have very active innovation units. What is your specialty?

'Many hospitals are betting on innovative technology; to name a few, Gregorio Marañon Hospital and Princesa Hospital in Madrid, Hospital Clínic in Barcelona, Parc Taulí in Sabadell and La Fe Hospital in Valencia.

'At San Carlos Hospital we very much deal with digital transformation of the healthcare system within society.'

Does social media have a role in this context?

'Social media brings us a lot of data to interpret individuals' behaviour and analyse their tastes, emotions, habits and interactions. It's a fantastic tool.

'A lot of physicians are very active on twitter, me included. I don't differentiate between my professional and personal life, I don't know how to do it. On twitter I fully express myself.'

Do you still have time left for surgery?

'I don't practice as much as I did. The problems and necessities you identify as a surgeon generate a sense of frustration and, at the same time, ideas on how to improve things.

'I have a vision for the hospital and I need innovation to transform it. Innovation is nothing but a tool to transform healthcare systems and society.

'Right now there isn't one healthcare system in the world that's ready to make the necessary changes. Technology is just one part of the change and mentalities must also evolve. Let's hope they do soon.'

Julio Mayol MD is Professor of Surgery at Complutense University, Madrid Medical School. He also serves as Medical Director and Head of the Innovation Unit at San Carlos Hospital in Madrid. The professor is the author of a fiction novel La guardia del Dr Klint (currently for Kindle) and is working on his second book.

Who – or which – will win the diagnostic laurels?

Man versus computer analysis

Report: Michael Krassnitzer

The recipe for an exciting congressional session is simple: Take a controversial hypothesis, a proponent who defends this hypothesis and an opponent who argues against it. The 33rd annual meeting of the European Society of Magnetic Resonance in Medicine and Biology (ESMRMB – in Vienna, in Autumn 2016) was the scene of a hot debate: 'Man versus machine in Radiology: the computer will take over'. Wiro Niessen, Professor of Biomedical Image Processing at Erasmus University Rotterdam, had the task to substantiate that proposition.

Anything you can do artificial intelligence can do better

'The computer will take over from the radiologists,' he declared, believing that machine learning, a form of artificial intelligence, could take over the interpretation of radiological images in about 20 years' time. He reminds us that more than a decade has passed since the chess programme Deep Blue succeeded in beating the former world chess champion Garry Kasparov. And, only recently, the AlphaGo programme beat the world's best Go player, Lee Sedol. Formerly, playing the Japanese board game had been considered too complex for software programmes to master. 'Anything you can do, artificial intelligence can do better,' Niessen emphasises. 'Algorithms get better and better and there is no reason why this process will stop,' he argues.

Learning strategies are also constantly improving, and the amount of data that machines can learn from also grows continuously. Truthfully, there is no competition in being better at looking at an image: 'Combining so much data is the computer's job,' the Dutchman stresses. 'Imaging now contains too much information for humans.'

Lastly, he asks if the most informative images are those that can be visually represented. MRI fingerprinting, MR spectroscopy and multiparametric images deliver results that can no longer even be adequately visualised.

'We couldn't do half the work that we do on a day to day basis without computers,' admits Adrian Dixon MD, Professor Emeritus of Radiology of the University of Cambridge. However, the British radiologist, who self-deprecatingly describes himself as a dinosaur, states: 'the computer will not take over'.

First he refers to interventional radiology: 'I doubt whether the computer will ever be able to master this.' But humans can also not be eliminated from purely diagnostic radiology. Dixon is convinced that any computer cannot replace the teamwork between radiographers, physicists and radiologists. But, although we have to move away from current standards in imaging, the computer is reaching its limits. He uses an example of a motorcyclist after an accident, who must not be moved because of possible injuries to the cervical spine and whose spine therefore can often only be viewed from unusual angles. Additionally, there are no standards at all when it comes to abdominal imaging, Dixon emphasises: 'There is no such thing as a normal abdominal CT.'

The computer will not take over radiology

This British radiologist is pleased about all technological support for mammography prompts, lung/liver nodule prompts, measurements to resize/perfusion/fat etc., multiparametric analysis, smoothed images, decision-making assistance and structured reporting – 'But, he insists, 'the computer will take over a lot of aspects of radiology, but will not take over radiology.'

The growing role and value o

Future professionals across E

Report: Fabrizio D'Abate and Angelo La Leggia

Ultrasound is often the first line of imaging used in the diagnostic pathway of a patient's journey into hospital. Additionally, the increased prevalence of chronic conditions and changes in the demographics of the general population has led to an increased demand for ultrasound. Fast-growing advances in technology also shift ultrasound into a more prominent role in patient diagnosis and clinical management. Ultrasound finds application in the prevention and diagnosis of a variety of conditions.

However, the safety and accuracy of ultrasound assessments need appropriate training and extensive experience of the operator. These are the reasons behind the development of the role of sonographers. A sonographer is a healthcare professional (non-medical doctor) who specialise in the use of ultrasound technology to produce diagnostic scans that will be integrated in the diagnostic process to help the medical doctor to formulate the final diagnosis.

This profession is well established in the USA, Canada, Australia, New Zealand and most of all in the United Kingdom, where the healthcare system heavily relies on these professionals. The UK appears to represent a unique reality in Europe, and in the world, where such professionals are entitled to not only perform an ultrasound examination but are also responsible for interpretation and reporting of the ultrasound findings.

Professional certification

The requirements for clinical practice vary greatly from country to country. Because of the high levels of decisional latitude and diagnostic input, sonography requires specialised education, often at postgraduate level through a master's degree.

Many countries require medical sonographers to have professional certification.

Sonographers must understand physics, cross sectional anatomy, physiology and pathology as well as understand the symptoms and treatments involved in the condition.

The areas of specialisation vary, some of which include: cardiology, vascular medicine, musculoskeletal, abdomen, soft tissues and small parts, obstetrics and gynaecology, paediatric, and neurology. The reality of sonographers across Europe is heterogeneous and is restricted to a few countries; sonographers now practice in Sweden, Denmark, Italy, Portugal, Norway and The Netherlands – some as part of pilot studies. Furthermore, physicians in Germany are beginning to view UK ultrasound services with interest and some countries are exploring the possibility for sonographers to be responsible for the interpretation and reporting of the findings as well.

The majority of sonographers employed in the Mediterranean countries fall mainly within the field of cardiology and vascular surgery. The lack of a uniform, pan-European, standardised structure for ultrasound training has been compounded by inconsistent regulatory norms across countries. This has negatively impacted the quality of technical training and the level of professional competency.

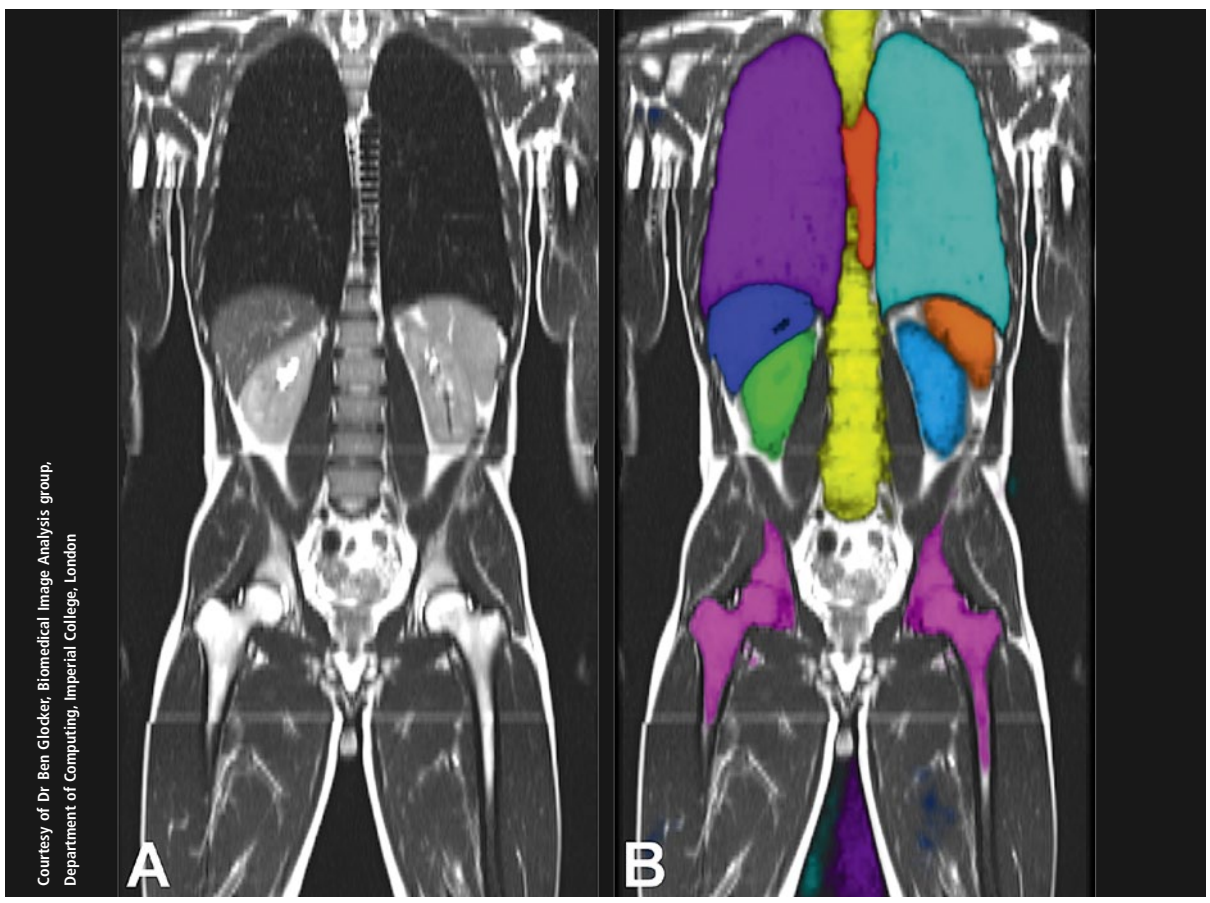
With rising demand for faster, economical ultrasound exams, the lack of skilled, trained and qualified sonographers is intensifying pressure on clinicians. The specific lack of these competent healthcare professionals across Europe is related to the fact that, although in most European countries ultrasound is taught during residency to doctors only, there are no uniform stand-

Angelo La Leggia MSc PhDc is a clinical scientist, specialised in Echocardiography. He gained a BSc in cardiac physiology at the University of Milan, and then focused on cardiovascular imaging, obtaining an MSc in cardiovascular sonography. He then gained another MSc in healthcare science and is completing his PhD in Clinical Research in Cardiology 'as a result of my great passion for research'. La Leggia spent eight years in the cardiovascular department in Legnano, Italy and moved to London in May 2016. He is now a specialist echocardiographer at the Royal Brompton Hospital. His interest lies in 3-D echocardiography and Speckle Tracking imaging in valvular pathology, specifically in patients undergoing interventional and surgical repair.

Recognising pattern, predicting survival

Machines are learning fast

Language recognition on the smartphone, spam filters in the e-mail programme, personalised product recommendations by Amazon or Netflix – all share one feature: they are based on an algorithm that recognises patterns in a set of data. This artificial generation of knowledge is called machine learning.



Courtesy of Dr Ben Glocker, Biomedical Image Analysis group, Department of Computing, Imperial College, London

Report: Michael Krassnitzer

Radiology, in which huge data volumes are produced, is an increasingly important playground for machine learning. The analysis of quantitative image features in large medical databases is meant to allow statistic descriptions of tissue characteristics, diagnoses and course of diseases.

At Imperial College, London, for example, a system called MALIBO (MAchine Learning In whole Body Oncology) is being developed that aims to detect tumours in whole-body MR images – without human intervention. So far, the system has looked at whole-body MRI scans of healthy volunteers to learn to identify organs and their components. The 'teachers' are radiologists who marked and named the structures to be recognised in the MRI scans. This enabled the systems to identify organs and their components fully automatically in new whole-body MRI scans.

Two different methods of machine learning were tested in this project: the principle of artificial neuronal networks that simulates the interaction of neurons in the brain, and so-called classification forests, i.e. large volumes of parallel decision-making paths. The former method was found to be superior to the latter.

High-resolution whole-body MR image of segmented structures

In the meantime MALIBO has entered phase 2, the recognition of primary tumours. 'We have seen some good results in the detection of colorectal cancers,' Dr Amandeep Sandhu Meng MBBS, a radiologist on the project team, reported.

Training an algorIthm using 200 images

This ambitious research project is but one among many presented in the session on machine learning at the European Congress of Radiology (ECR 2017) in Vienna from 1- 5 March 2017.

A team at the University of Valencia (Spain) developed an algorithm that can identify and characterise individual vertebral bodies on CT scans of spinal columns. The algorithm, which was 'trained' on 200 images of healthy and diseased spinal columns, assesses 90 percent of scans it has not previously processed correctly.

At Bari University (Italy) a research team evaluated a computer-assisted decision-making system (CAD),

urope

Fabrizio D'Abate MSc is a Clinical Vascular Scientist and member of the Society of Vascular Technology of Great Britain and Ireland. He gained his MSc in Vascular Ultrasound and MSc in Clinical Experimentation of Drugs in Florence-Italy, spent a year at the vascular research institute in Exeter, UK, studying the micro and macro vascular complications of diabetes with non-invasive technology, and is now a senior Clinical Vascular Scientist at the prestigious St George's vascular institute, St George's Hospital, London, where he is responsible for non-invasive imaging within vascular surgery. His clinical/ research interest in diabetes-related vascular complications and imaging, sport related vascular conditions (iliac endofibrosis, popliteal artery entrapment), abdominal aortic aneurysm screening programs and thoracic aneurysm. He is an active member of the INSITE (International group of expert for the detection and management of Iliac Endofibrosis).

ards in quality assurance and no minimum standards for the teaching syllabus.

As mentioned by Professor Christian Arning MD (Medical Director of the Neurology Department at Asklepios Klinik Wandsbek, Germany) in 2008 on Healthcare in Europe, the qualifications required of an instructor in this field have not been established in the residency regulations. As a result, quite often one resident will pass on their partial knowledge to the next.

For ultrasound, the operator's experience is of paramount importance. While physicians should have the knowledge and skills in ultrasound, sonographers should present as a dedicated profession to ultrasound and work in combination with physicians for the patients' benefit.

The use of sonographers has potential in promoting screening programmes within the medical specialties, reduce waiting lists for patients to have access to an ultrasound service, reduce the number of more advanced and expensive imaging modalities (reducing patient's radiation exposure) and reduce hospital lengths of stay and related costs.

Employing sonographers would enable doctors to dedicate and commit more time towards the patients' care thus optimising the competences of different healthcare professionals and share responsibilities.

Gaining a dedicated space within societies

Another advantage: the cost and time of sonographer training would be lower. Overall, several initiatives have begun to promote the sonography profession across Europe with a dedicated space for sonographers in societies such as the European Society of Vascular Surgery; the European Society of Echocardiography and the European Federation of Ultrasound in Medicine and Biology.

Despite all these advantages, there are still some challenges that are moderating the evolution of such a profession: the level and control of competencies and the practice of such new activities for sonographers.

It is desirable that the European countries develop a uniform dedicated education programme to develop sonographers and see these professionals as a valid aid in healthcare – rather than the competitors of clinicians.

developed to detect breast cancer lesions. Of 3,735 scans, 192 were considered suspicious, 102 were false positives, and four were false negatives. This promising predictive ratio would allow the CAD system to identify from large volumes of scans those breasts that do not require further examination.

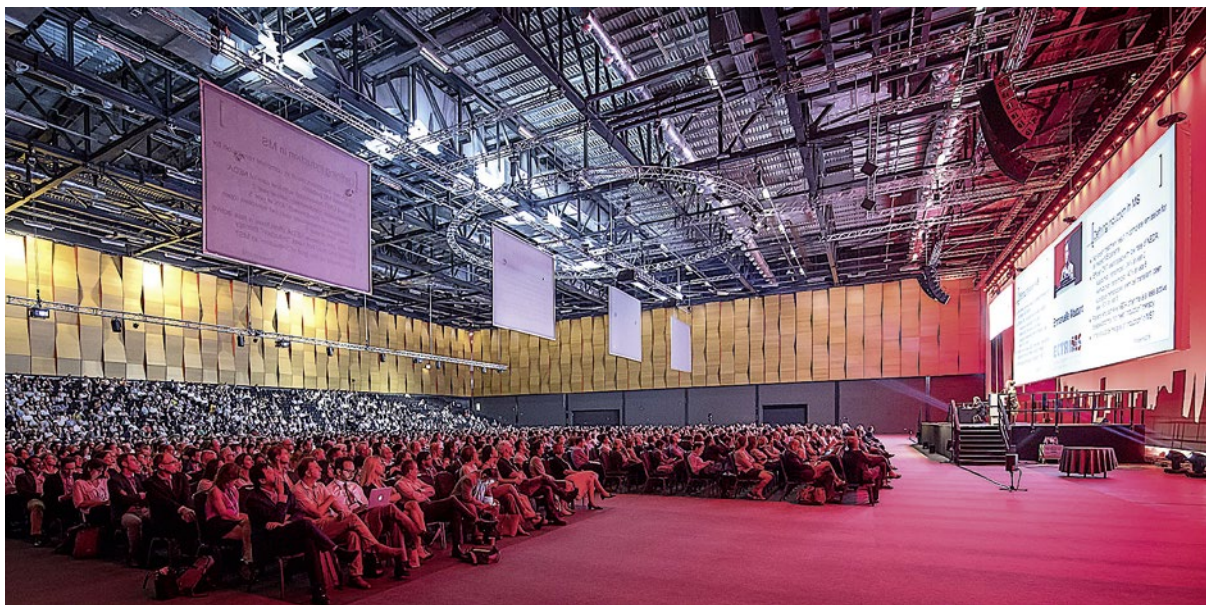
Teams at the University Hospitals of Zurich and Basle, Switzerland, jointly developed an analytical tool that can predict osteoporosis risk from a multitude of radiological images from different sources and varying quality. Working with CT 179 images, dyed by radiologists, from 60 patients, the neuronal network learned to cull quantitative bone data. Moreover, at Basle University Hospital, PACS Crawler was developed – software to predict osteoporotic fractures risk from looking at CT scans

Last, but not least, a research team at Mainz University Hospital developed an algorithm to predict liver transplant patient survival based on pre-operative 3-D CT scans. In 80 percent of the cases the algorithm correctly predicted which patients would survive surgery for more than one year. Strangely enough, the researchers don't know how the algorithm arrived at its decisions. 'That's a bit like a crystal ball. We have no idea how it works – but it does work,' said Dr Daniel Pinto dos Santos, Head of the research team Radiology Image and Data Science (radIDS).

Seeking an efficient therapy for the progressive stage of MS

PET offers new multiple sclerosis insights

Positron Emission Tomography (PET) is helping to provide MS experts some insight into what drives progression of the disease. PET also has the potential to quantify the effects of new, targeted therapies on MS patients, according to consultant neurologist Professor Bruno Stankoff.



Report: Mark Nicholls

The role of PET was among the key topics at the recent European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) annual congress, held in London. Speaking after his presentation 'PET imaging of cellular and molecular abnormalities in MS' at the congress - which is a dedicated platform to promote and enhance research in MS – neurologist Professor Bruno Stankoff expanded on the potential of PET in advancing knowledge and treatments of the condition.

PET, he said, might offer an insight into an 'improved comprehension of what drives MS progression', whilst also shaping the development of new treatments. 'These are not therapies targeting relapses but targeting root mechanisms and,' he added, 'with PET used to evaluate the effect of some therapies that promote endogenous myelin repair, decrease neuro-inflammation or decrease neurodegeneration.'

MRI remains a proven modality in the diagnosis of MS, but PET has the advantage of enabling very specific imaging directed to cellular or molecular components. 'PET is very specific, very sensitive to changes and we can quantify the image,' explained Stankoff, who is a consultant neurologist at the MS Centre, Saint-Antoine Hospital, Paris. 'We have taken advantage of technique to approach some biological mechanisms that could identify MS pathophysiology and MS progression.'

In his on-going research with PET for MS, Stankoff and team have sought to quantify the dynamics of myelin loss and repair; image neuro-inflammation related to innate immune cells, and the use PET to quantify the normal compartments of neurodegeneration in core different stages of the disease. 'By focusing on these we might quantify two of the main mechanisms that can drive progression of the disease, the success or failure of endogenous lesions repair and the level and localisation of neuro-inflammation,' he explained.

While stressing that the work is still at the research stage rather than in daily clinical practice, he suggested that the benefits to patients would become clearer in the mid- or long-term, rather than the short-term. 'The benefit is shortening of the timeframe to develop some efficient therapy for the progressive stage of the disease,' Stankoff explained, adding that, so far, results are promising and PET has already provided some important answers in the field of MS.

With individual patients, it can show how some people can repair their lesions while others are not so strong in terms of remyelination, but this may help in prognosis when the disease is diagnosed by better identifying the patients who will need treatment to promote lesion repair.

Another key finding is in quantifying neuro-inflammation in patients with different forms of MS, which he believes may offer a marker of progression – that those with more inflammation may be more prone to having a progressive form of MS.

The team is working on a study that combines PET and MRI to develop and assess a new imaging biomarker that has the potential to be used as an index of neurodegeneration in multiple sclerosis. PET and the isotypically radiofluorinated form of Flumazenil (FMZ) will be used to assess neuronal damage at the early phase of either relapsing or primary progressive MS.

Professor Bruno Stankoff is a consultant neurologist at the MS Centre, in Saint-Antoine Hospital, Paris, and co-head of the team researching myelination and remyelination in the CNS: mechanisms, imaging and therapy, at the Brain and Spinal Cord Institute (ICM), in La Pitié-Salpêtrière Hospital. He leads several projects aimed at imaging remyelination, neurodegeneration, and microglial inflammation in MS.

* Research across long-term effects and prognosis, imaging techniques, B-cell depletion therapies, personalised care, immune response and progressive MS was presented at ECTRIMS 2016 (London, UK. 14-17 September). The congress themes included understanding the mechanisms of disease progression; new research findings including immune and mitochondrial abnormalities; approaches to early treatment; evolving approaches thanks to better understanding and personalised treatment; long-term treatment effects and prognosis; new insights from registry and cohort studies; new directions in progressive MS research; imaging neuroprotection and repair, and advances in imaging techniques.

Latest ac might no

Current advances such as phase-contrast CT are taking medical imaging further but their use in clinical practice may have to wait up to a decade, prominent physicist predicts.

By Mélisande Rouger

Cooperation between medical specialists and biomedical engineers is having a fresh start as healthcare professionals were invited to the annual meeting of the Spanish Biomedical Engineers Society (CASEIB 2016) in November in Valencia.

Researchers and key representatives from all across the country shared expertise during dedicated roundtables and sessions to try and tailor technological advances to current healthcare needs, notably in medical imaging. During the meeting, José María Benlloch, a professor of investigation at the Spanish Superior Council for Scientific Investigation at Valencia Polytechnic University, presented the newest advances in medical imaging techniques. The long held perception that CT is better for hard tissues imaging and MRI better for soft tissues is about to become history, according to Benlloch, who obtained the Spanish National Investigation Award in 2014 for applying particle physics techniques to molecular imaging in biomedicine. However, years will pass before some of these improvements can benefit population healthcare, he believes.

'Phase-contrast will change the paradigm and bring CT into soft tissue imaging. However the technique will not enter clinical practice before 10 to 15 years, because we first need a coherent source of X-rays. I believe X-ray techniques using laser will become such a source and will be much more affordable in the future.'

Unlike CT spectroscopy, a mature technique that will enter clinical practice in three to five years according to Benlloch, phase-contrast CT is still facing a number of technological challenges. For X-ray detectors to be sensitive to phase-contrast, resolutions in the one micrometer range are needed. Researchers are working on these developments, but they still have a long road ahead.'

'We can achieve this resolution by placing a rack on detectors with poorer resolution, but in doing so we lose a lot of X-ray power. Clearly significant technological advances are still lacking for the technique to become financially available and be used in most hospitals,' he said.

MRI's trademark difficulty in imaging hard tissues could soon be solved as well, as Benlloch and his team are currently working on MRI solutions for dental applications, in which dentists could not only see teeth but also the surrounding soft tissues.

'This is very interesting for dentists because it will not use radiation. They will be able to image gums and things that are now almost invisible on X-ray,' he said.

This new MRI development uses a permanent magnet applied to only a small part of the body. It also uses a

Phase contrast CT still faces several technological challenges

dvances in CT, MRI & PET ot enter clinic soon

Jose Maria Benlloch is a professor of investigation at the Spanish Superior Council for Scientific Investigation (CISC) at Valencia Polytechnic University and Director of the Instrumentation Institute for Molecular Imaging at CISC. He received the National Investigation Prize in 2014 for his relevant contributions to the application of particle physics techniques to molecular imaging in biomedicine. Benlloch wrote his PhD thesis in 1990 on detector development and data analysis in the DELPHI experiment of the LEP collider at CERN in Geneva, Switzerland. He has been on the research staff at the Massachusetts Institute of Technology under the supervision of Physics Nobel Prize holder Jerôme Friedman and has published over 200 articles in international publications. He has coordinated 30 research projects and has eight patents and three spin-off companies in biomedical engineering.

low electromagnetic field and does not occupy as much space as current scanners.

Acquisition time will be just a minute and the system will be automatised so that dentists can read the scans themselves without the help of an MR specialist.

The cost will also be significantly inferior to traditional MR scanners - €120,000, experts estimate. The technique should be ready by the end of 2017, and available in clinic in two to three years if it receives FDA and CE marking.

In PET imaging, the US National Institute of Health has recently granted $15 million to California University UC Davis, Berkeley University and Pennsylvania University to develop a true whole-body PET/CT scanner enabling to image the patient in 2 minutes while significantly reducing dose.

'This will improve sensitivity in diseases and tumors detection and enable to acquire dynamic pictures of the whole body. We will be able to see biology as never before, for instance we will be able to see how molecules evolve from one part of the body to another and in how much time, we will have temporal resolution. Being able to see these correlations in real time will bring much more information than what we currently have,' Benlloch said.

The fact that radiologists are coming to the congress will help engineers better understand the needs of their colleagues, the researcher believes. 'It is better that radiologists participate from the start so that we don't lose time building a machine they may not need.'

'Cooperation between doctors and engineers is absolutely necessary for the investigation and the development of new technologies that improve citizens quality of life. The doctors in their daily clinical practice may detect the limitations of current technology and the problems to be solved, and from that information the engineers can offer solutions and improvements. To be efficient, this process needs a very tight cooperation between both parties, and the relatively recent introduction of the biomedical engineering specialty in Spain will impulse in this direction,' Francisco Javier Saiz Rodriguez, president of CASEIB 2016 organising committee, echoed.

The Spanish Society of Radiology (SERAM) will also welcome biomedical engineers during its next biannual meeting in 2018, as the congress scientific committee will dedicate an area to biomedical engineering, making it an important line of the meeting.

'For us this strategic positioning. There are many on-going cooperation projects between the two specialties in Spain, but we don't have a registry yet. We are still very much unaware of what is being done and what could be done with biomedical engineering. There are many areas of cooperation that we could work on, such as Big Data use, standardisation of new techniques and image acquisition itself – for instance to obtain an image of the heart without performing apnea in some cardiac settings. I think our cooperation is just taking off,' Àngel Gayete, SERAM President, said.

Clinicians define an optimal approach for MRI contrast

The CBCA satellite symposium

Gadolinium-based contrast agents are an essential component of MRI exams, but are challenged by findings of residual depositions of gadolinium in the body, even though the clinical relevance remains unknown. Three clinicians described how changes to MRI protocols and dose levels for contrast media can optimise the balance between benefit and risk for patients and radiologists.

Dr Francesco Sardanelli

Dr Luis Martí-Bonmatí

Dr Josef Vymazal

For magnetic resonance imaging (MRI) examinations the use of gadolinium-based contrast agents (GBCAs) is essential to detect and characterise cancerous tumours and delineate and assess vascular disease. The safety profile of GBCAs has always been considered highly favourable with few relevant contraindications and a lower rate of acute adverse reactions than are seen for iodinated contrast agents used for X-ray based imaging.

When an association between GBCAs and nephrogenic systemic fibrosis (NSF) was described in 2006, confidence was shaken, provoking a debate regarding the risk versus the benefit of these compounds. Thanks to well-documented studies and changes to MRI protocols, the debate subsided and, since 2009, no further cases of NSF have been reported. However, debate was re-ignited in 2014 with the first reports of increased signal intensity in the brain after the administration of these agents.

To provide an update for radiologists at the European Congress of Radiology (ECR 2017, in Vienna) on the use of GBCAs and how they can best optimise the balance between risk and benefits, three prominent experts presented insights into the current state of the debate during a satellite symposium hosted by Bracco Imaging.

Dr Francesco Sardanelli, Professor of Radiology at the University of Milan, Director of the Department of Radiology at the Research Hospital Policlinico San Donato in Milan, Italy, said: 'In a context where our knowledge is still limited and confusion and false simplifications make our practice more difficult, we need to continuously re-evaluate the available evidence and to make careful clinical judgment of the profile of each individual patient. The future will be a less standardised approach for gadolinium-based contrast agent usage, an application of personalised medicine to the field of MRI.'

The emergence of findings for NSF came in the context of what Sardanelli compared to a 'perfect storm' yet had a positive impact on clinical practice, because it forced radiologists to rethink the value of unenhanced MRI, to better apply technical tools for accurate diagnosis, to screen for renal failure patients as candidates for GBCA injection, and to accurately describe the type and dose of contrast agent for each patient.

The current discussion, he said, focuses mainly on gadolinium accumulation in the brain, yet the clinical relevance of the findings remains unknown. At this point, no clinical consequences, and no neurological symptoms have been associated with brain signal increases in patients who were injected with GBCAs.

'The high impact that this message has is that brain is brain,' he noted, outlining key points for balancing diagnostic performance with safety. First is to rethink the indications for GBCAs. Where one in three MRI examinations today includes contrast-enhanced scans, a reassessment of the necessity of a GBCA injection, 'could reduce this rate, but probably it will be difficult to go below one in four'. A second issue is to take into consideration the age and clinical profile of the patient, he said, while radiologists might also rethink the GBCA dose to determine if less is better.

On this point, **Dr Luis Martí-Bonmatí**, director of medical imaging at La Fe University and Polytechnic University Hospital in Valencia, Spain, discussed the potential for determining an optimal approach in the use of gadolinium contrast agents in order to achieve the maximum benefit. Acknowledging the concerns, he said, 'It is relevant to recognise the extremely important role that contrast-enhanced MRI studies have in defining the presence and characteristics of so many different diseases and pathologies. The issue then becomes how to strengthen contrast enhancement across most indications that require contrast injection to achieve the highest diagnostic confidence.'

Martí-Bonmatí focused on the contrast agent property known as relaxivity, a measure of the degree to which a given amount of contrast agent shortens the T1- and T2-weighted relaxation times of tissue and how these values can be exploited depending on the clinical need, to increase enhancement or to lower the dose of the agent used.

Not all contrast agents based on gadolinium are equal, he noted. Three chelated compounds are categorised as high-risk for NSF, while five others, are classified as medium- or low-risk in Europe. Regarding gadolinium depositions in the brain the current evidence is inconsistent.

In all cases high-risk chelates and double or triple dose administrations are to be avoided, particularly for patients with renal insufficiency. Using lower-risk gadolinium chelates the lowest dose should be administered to obtain the clinical information required. On this point he demonstrated how the selection of an appropriate contrast agent and use of higher field strength can maximise clinical information while minimising the risk for patients. Contrast media with high relaxivity allow the maximum visual enhancement, depiction and characterisation, enable the use of low doses and thereby assure the greatest possible benefit for both the patient and clinician.

Dr Josef Vymazal from Na Homolce Hospital in Prague, Czech Republic, said he is 'deeply convinced that this is still a work in progress and we should be very careful about conclusions drawn about the topic of gadolinium deposition'. He emphasised that the mechanism by which GBCAs penetrate into the brain is still not understood, and to this point no clinical manifestations have been described in connection with the phenomenon.

The unique properties of gadolinium are what have made this metal in a chelated form an essential part of almost all MRI contrast agents, he explained. In an analysis of published and presented works, Vymazal showed that, as yet, there is no data available on the chemical form in which gadolinium is deposited and that work is needed to elaborate this. In addition, the potential contributions of other metals known to reduce T1 and T2 relaxation times and to deposit in deep nuclei of the brain, such as iron, copper and manganese, have not yet been assessed, he said.

Building on these findings, in a study completed just days ahead of the ECR congress, Vymazal opened a path for further clinical investigation on what he called a new concept focused on 'gadoferritin' or gadolinium-ferretin complexes, a compound developed at the Institute of Organic Chemistry and Biochemistry in Prague. Signal intensity reported in deep-brain nuclei may be explained by the presence of such gadolinium-ferretin complexes, the study suggests.

In the end, he stated, it is possible that the chemical form in which gadolinium complexes are retained in the various brain areas may vary over time, and more than one form may coexist at the same time.

In summary, Vymazal noted that while gadolinium deposition in various organs, including brain, bone, skin and liver, has been demonstrated by pathological evidence for all GBCAs, including both linear and macrocyclic agents, at this time there is insufficient evidence to allow conclusions to be drawn concerning the clinical impact of this phenomenon.

The latest cardiac devices feature MRI AutoDetect

Cardiac device patients can be scanned

Recent technological advances have generated a wave of MR-conditional devices that increase patient access to often crucial MRI scans. However, the processes involved in system selection and configuration before and after MRI scans can prove to be time-consuming and complex. Biotronik provides various possibilities to maximise patient access to MRI while streamlining workflows for clinicians.

Automatic recognition of MRI zone

To simplify processes for clinicians, devices in the latest range of pacemakers, ICDs and cardiac resynchronisation therapy devices feature MRI AutoDetect – a technology that enables the device to automatically recognise when it is in an MRI environment within a programmable time window of up to 14 days. When an MRI environment is sensed, the device automatically converts into MRI mode and then returns back to full functionality after the scan is complete. This reduces the number of patient visits required to configure the device and also minimises the duration of reduced therapy.

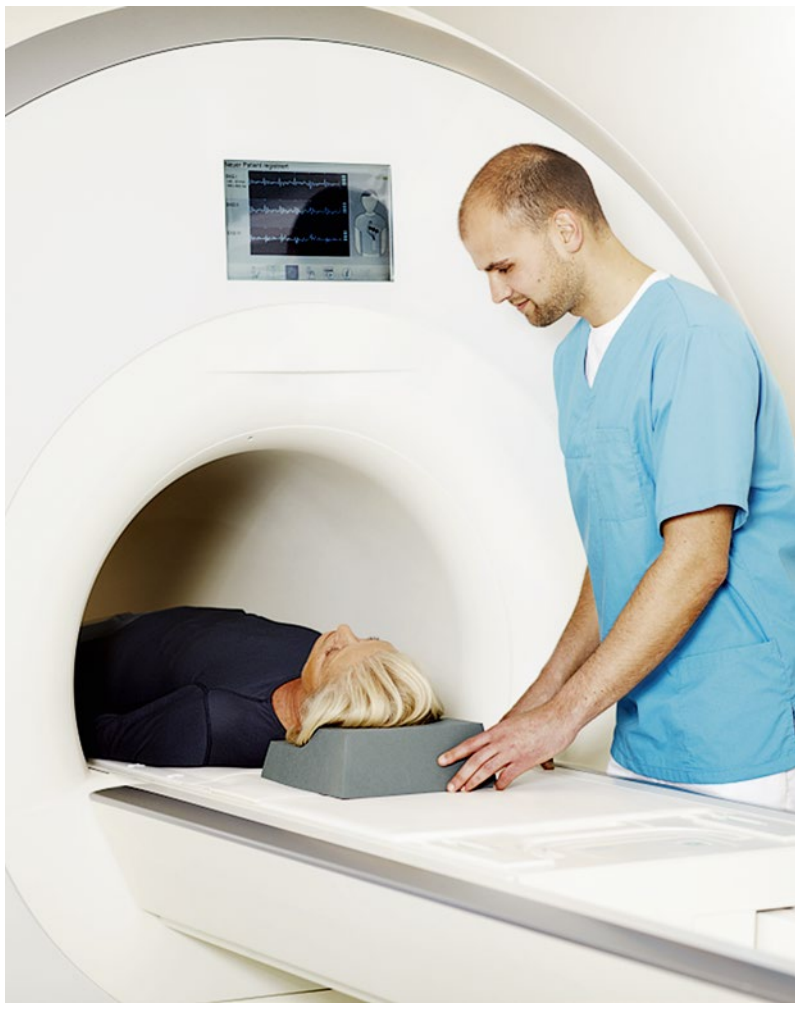
Increased MRI accessibility

Dr Geraint Morton, at Portsmouth Hospitals NHS Trust, United Kingdom, emphasises the importance of MRI access. 'Cardiac patients with comorbidities such as neurological diseases, or orthopaedic conditions, often require MRI, so it's essential to maximise accessibility. The care and management of comorbidities can be compromised in many cases if patients can't have an MRI scan.'

In addition to the existing approval of 1.5-T MRI scans with full-body scanning options, Biotronik recently received CE approval for 3.0-T full-body scanning with devices in its latest range of MR-conditional pacemakers. As a result, clinicians have more flexibility to perform high field strength MRI scans without any scanning area restrictions. This can be especially important for patients with comorbidities such as cancers or single- or multi-vessel disease in patients with coronary artery disease, which can require in-depth examination of tissue in anatomical regions that might previously have been restricted.

Biotronik develops ProMRI portfolio online tool

'To further ease the complexities surrounding MRI for cardiac patients, Biotronik recently introduced the online tool ProMRIcheck.com, which enables physicians to verify the MR conditionality of Biotronik device systems prospectively or retrospectively to implantation,' the company reports. 'With the world's largest range of implantable cardiac systems approved for MRI scans in its ProMRI portfolio and a variety of accompanying technologies, Biotronik improves MRI accessibility for cardiac patients while simplifying the processes involved for clinicians.'



Drive to standardise lab tests moves into complexities of endocrinology

A mandatory comparability of results

Following its success in establishing reference methods and values for a range of simple molecules, International Federation of Clinical Chemistry and Laboratory Medicine's Scientific Division takes on the challenge of harmonization for hormones and endocrine tests.

Report: John Brosky

As Professor Philippe Gillery takes up his role as Chair for the Scientific Division of the International Federation of Clinical Chemistry (IFCC) and Laboratory Medicine he is pleased to note there is, at this moment, a greater interest in cooperation among the various stakeholders for the drive toward a standardisation and harmonisation of results, which was not always the case. 'It's true that until recently many laboratories continued using methods established many years ago and considered that, when (and perhaps because) they are a university centre, they were doing a good job. Now this is changing,' he explains.

According to Gillery, colleagues in clinical labs are increasingly aware of the importance of comparability of results from the evaluation and analysis of assays, and in those countries where laboratory accreditation according to different ISO norms is now mandatory, harmonisation of standards is understood to be crucial to that process.

Among manufacturers, he said, the chain of traceability and value assignment for assays was not always strictly controlled because reference measurement procedures and materials were lacking, such that the resulting values for similar tests were not the same for all manufacturers. This has also changed.

A global regulatory pressure

Among manufacturers there is a global pressure exerted by regulatory bodies, as well as a greater visibility of the process of standardisation undertaken by IFCC, which has helped demonstrate the importance of having common procedures and common reference systems.

Having accepted the benefits of standardisation, manufacturers now work closely with the IFCC Scientific Division with a goal of harmonising assay outcomes.

Laboratory colleagues, manufacturers and experts from diverse institutions, 'all have to go in the same direction, which is to improve the comparability of results from one laboratory to another laboratory, as well as, over time, for the same patient,' Gillery said.

The first efforts of the IFCC Scientific Division, which focus on relatively simple molecules such as creatinine or cholesterol, have borne fruit.

A landmark achievement was establishing a reference measurement procedure for Haemoglobin (HbA1c), which is routinely assayed in patients with diabetes mellitus. 'Today this is the only international anchor for HbA1c, which guarantees the comparability of results all over the world. This is a success for the monitoring of diabetic patients, as well as for the diagnosis of diabetes, and all manufacturers calibrate their assays against this reference measurement procedure,' he said.

The IFCC Scientific Division is currently working in a more complex area, devoting its efforts to more complicated molecules, especially peptides, through its different Committees and Working Groups.

An update on this work will be presented during EuroMedLab 2017 in Athens where Gillery will lead a two-hour symposium on standardisation in endocrinology. Following an overview of the Division's progress to date, the discussion will focus on advances towards harmonisation of results of laboratory tests used to explore endocrine functions through assays for growth hormone, parathyroid hormone and thyroid hormones.

The hormones present unique challenges to the clinical community for standardisation or harmonisation, he said, and the presentations will aid colleagues in gaining an appreciation of the issues as well as the achievements to date realised through cooperation and consensus.

Assuring sustainable standards

The IFCC Scientific Division's work aims to assure standards that result in a sustainable performance, and also that the established values are accepted by the clinical community.

'The clinical community is often less aware than the laboratory community that there can be a variability of values in assay results, and that there can be an imprecision in those values,' Gillery said. Because a patient typically goes to the same testing laboratory each time, clinicians are not concerned by the possibility that there are variations from one laboratory to another. Yet, patients move, and today may receive results from a laboratory in another city or another country that are completely different than those of previous tests.'

The benefit to patients of IFCC's effort is to assure consistent and comparable results regardless of where a test is performed, he explained, so as to establish common clinical thresholds across all methods.

Philippe Gillery is Professor of Biochemistry and Molecular Biology at the Faculty of Medicine, University of Reims Champagne-Ardenne, and Head of the Biology and Pathology Department of the University Hospital of Reims, France. He has served as President of the Société Française de Biologie Clinique and is currently Chair of the Scientific Division of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC_. He is Associate Editor of the Clinical Chemistry and Laboratory Medicine Journal and has published more than 200 articles in peer-reviewed journals.

Mandatory lab accreditation works in France

One for all and all for ISO 15189

Report: John Brosky

People working in clinical laboratories often believe their work is of the highest quality, and adhere to what they believe is the highest standard – which is their personal opinion.

This is challenging for anyone responsible for laboratory accreditation to international standards, according to Michel Vaubourdolle, Chair of the Société Française de Biologie Clinique (SFBC) working group on ISO Accreditation.

Their first difficulty is cultural, he explained. A clinical laboratory is a culture of specialists, each very different and not always willing to work with other groups and resisting the idea of a single quality management system that is applied to all groups equally. 'They see accreditation to international standards as a constraint, something that will cost money and, in the end, not be very useful. "Why?" they will ask. They will tell you they already work well, why should they now have to prove it?

'After 10 years of our efforts to meet accreditation standards, it's difficult to say that a laboratory now delivers something appreciatively better or different than before. What we can say is that, today, thanks to adopting standards for quality, we can at least prove the quality of our work. We can show that when there is an error we can rapidly correct it so that it does not occur again. We can easily show we have improved the management of laboratories. We can show there have been efficiencies in spending and cost savings,' explained Vaubourdolle, who is the Head of Department Biology-Pathology University Hospitals East Paris and Head of Service Clinical Biochemistry, Hospital Saint-Antoine, Paris. 'In the end, like many of my colleagues, I believe that the process of accreditation has brought many positive things and not had a negative impact,' he added.

At EuroMedLab 2017, held in Athens, in his capacity as an executive board member of the International Francophone Federation of Clinical Biology and Laboratory Medicine, Vaubourdolle presented France as a case study in the positive impact of accreditation.

There are many countries where accreditation is not mandatory, or linked to the reimbursement process, he explained. France is one of the five European countries to have chosen mandatory accreditation to operate a clinical laboratory, whether public or private, and for all tests, from genetics to haematology or clinical chemistry.

Prior to the reform there were 5,000 laboratories in France. Due, in part to mandatory accreditation, France has seen a dramatic consolidation in the sector, so that today here are 800 laboratories. Though Vaubourdolle notes the number of access sites for patients has remained the same.

The new model is for a single central laboratory to serve multiple sites, and this trend includes the massive public hospital structure in France so that smaller hospitals are now grouped with a single multi sites laboratory.

The consolidation has greatly helped the accreditation effort, he said, making it easier to evaluate and monitor a single operation against the requirements of the International Standards Organisation (ISO) rather than multiple independent laboratories.

The decision to make accreditation of laboratories mandatory and to link the accreditation to reimbursement was considered essential in order to accelerate the accreditation process. In one word, it worked, he said. By 2016, all laboratories had been accredited across half of their tests amounts, and the national roadmap calls for 100% conformity by all labs to the standards of ISO 15189 before 2020.

Mandatory accreditation also helped facilitate the integration of multiple smaller operations into a single and larger structure with shared resources, Vaubourdolle said. 'This is not always so easy, particularly in the public hospital sec-

Continued on page 13

The outgoing Chair of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) working group on ISO/Accreditation, **Michel Vaubourdolle, Pharm.D, PhD** is the current Chair of the French Society for Clinical Biology Working Group on Accreditation. An Executive Board member of the International Francophone Federation of Clinical Biology and Laboratory Medicine, he is also the President of the Triennnal International Symposium on critical care testing and blood gases.

Seeking greater harmonisation in laboratory medicine

Unifying recognition of professional qualifications

Improved harmonisation of laboratory medicine practice across Europe will help lead to better patient outcomes and produce comparable laboratory information irrespective of where and how the data have been generated, Mark Nicholls reports

With harmonisation regarded as a fundamental aspect of quality in laboratory medicine, it is high on the agenda of delegates to the EuroMedLab 2017 congress to be held between 11-15 June at the Megaron Athens International Conference Centre, Greece.

Harmonisation involves all the steps of the service (pre-analytical, analytical, and post analyical phase) as well as embracing aspects of the profession in a symposium hosted by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). This will provide four lectures dealing with the harmonisation of the pre-analytical phase, medical laboratory accreditation, the mutual recognition of professional qualifications across Europe, as well as continuous professional development.

Speaking to European Hospital ahead of the conference, Gilbert Wieringa, Chair of EFLM's Professional Committee, explained the importance of harmonising the recognition of professional qualifications. 'It's to ensure that laboratory medicine is practised to common standards, so that patient safety is protected irrespective of which country the specialist emanates from.

'Under EU Commission Directive 2013/55/EU – the Recognition of Professional Qualifications – harmonisation would extend opportunities for specialists to practice in other EU countries without having "compensation measures" imposed on them such as the re-taking of local professional exams; in turn it could also catalyse a more equitable distribution of skills and resources across the EU.'

Dr Wieringa will highlight how EU Commission Directive 2013/55/EU provides a passport to professional migration across EU borders for professions that can work to a Common Training Framework.

He will also point to EFLM holding a Register of 'Specialists in Laboratory Medicine'; how the organisation is pursuing recognition as a unique cohort amongst laboratory medicine practitioners, and how achieving recognition raises the profile of the contribution of laboratory medicine to better health and best care.

Formed in 2007 through the merger of the Forum of European Societies of Clinical Chemistry (FESCC) and the European Communities Confederation of Clinical Chemistry (EC4), the EFLM connects National Societies of Clinical Chemistry and Laboratory Medicine to create a platform for all European specialists in laboratory medicine.

A strong advocate of the Register of specialists, in adding weight to the argument for their recognition, in his talk Wieringa also intends to describe the backbone work that already carried out by EFLM and its predecessor organisation EC4 in setting standards for specialist practice, establishing the Register, an expected code of conduct, and adoption of the unifying term 'Specialist in Laboratory Medicine'.

He will offer guidance on how people can join the Register, as well as share an update on progress with implementation of the Recognition Directive at the EU Commission.

While medical staff already enjoys professional migration as members of the sectoral professions, the Directive offers equal opportunity to science and pharmacy trained specialists, once a Common Training Framework has been adopted by one third of the EU member states (i.e. 10). It remains unclear how long the harmonisation process will take, though EFLM is maintaining close contact with its leads at the EU Commission throughout.

The session will also hear from Wim Huisman, previously Head of the Laboratory for Clinical Chemistry and Haematology at the Medical Centre Haaglanden in Leidschendam; Ana-Maria Simundic, Professor in the Department of Medical Biochemistry at Zagreb University, and Elizabeta Topic, Professor of Medical Biochemistry at the Faculty of Pharmacy and Biochemistry University of Zagreb.

* The EuroMedLab 2017 ELFM symposium 'Harmonisation in laboratory medicine': 10.30am-12.30pm, 12 June. Venue: Skalkotas Hall, Megaron Athens International Conference Centre, Greece.

Gilbert Wieringa chairs the European Federation of Clinical Chemistry and Laboratory Medicine's (EFLM) Professional Committee and is clinical lead for Laboratory Medicine in Bolton, England. Formerly the healthcare scientists programme lead in the Department of Health, and Greater Manchester Primary Care Trusts' pathology lead, his main interests are in the provision of antenatal screening services, quality assurance for 'high street' diagnostics and the harmonisation of growth hormone measurements.

MiniCollect weds carrier tube

Since autumn 2016 a small tube has been making daily life easier for users and patients. A simple but effective addition now offers many new advantages in analysis, the manufacturer reports.

Following the successful launch of MiniCollect, a new capillary blood collection system, Greiner Bio-One has launched the tube MiniCollect Complete to simplify the analysis process.

For centrifugation, MiniCollect tubes can be threaded into a Premium carrier tube using a simple rotational movement, the Austrian manufacturer Grenier Bio-One reports. 'In the Complete version, the MiniCollect tube is already irreversibly assembled in the carrier tube. This brings many advantages for sample analysis in instruments.'

When combined, the dimensions correspond to a standard 13 x 75 mm tube format, the firm adds. 'This allows the tube to be placed directly into a standard centrifuge adapter. Previously, it was necessary to adjust the settings on the analysis device, because the tube format was different for venous and capillary blood samples. The combined tube means that both capillary and venous blood samples can now be analysed in the same way, without complex modification of the device.

'Another advantage is that the carrier tubes can be identified using standard label formats. MiniCollect Complete are primary tubes. Both blood collection and subsequent analyses can be carried out using the same tube. It is not necessary to transfer the sample material to a secondary tube for analysis.'

The tube also has a new cap. 'The membrane can be pierced by a cap-piercing analysis needle while the cap is closed, before automatically resealing after the needle is removed,' Greiner adds. 'The caps are completely sealed, meet the highest standards and can be sent via pneumatic post with confidence, and without losing any sample material.'

Combined filling volume and integrated blood collection scoop

Combined filling volumes for the EDTA and serum tubes make the preparation of samples more straightforward, the firm points out. 'Two easily visible filling marks on the tube provide greater flexibility for use. It's no longer necessary to decide on a certain volume in advance, which reduces logistical efforts.'

The blood collection scoop integrated into the wide tube opening enables the drop of blood to be transferred to the MiniCollect primary tube quickly and easily, minimising adhesion. 'The sample immediately comes into contact with the additive inside the tube.'

No to unnecessary agitation

The sight of a puncture needle often causes anxiety in children. 'One of the main advantages for our young patients is that the safety mechanism of the MiniCollect safety lancets means that no needle is visible at any point before or after the puncture. This makes the situation more relaxing for all involved,' explains Petra Langmayr, former paediatric nurse and product specialist at Greiner Bio-One. After the puncture, the needle retracts automatically and is safely enclosed within the plastic casing. The risk of needlestick injuries is prevented.

* Product availability depends on country-specific registrations.

Use less blood for analysis

The patient blood management concept

Blood is a very special juice' – something even Goethe's Mephistopheles knew. Medics have also known this for centuries, so it's nothing new that the 'juice' and its properties receive a lot of attention in medicine. However, what is new is that dealing with the use of blood through patient blood management (PBM) is coming to the fore.

Report: Anja Behringer

PBM was developed with the help of data from the first Austrian benchmark study in partnership with international experts. The concept is now implemented in Western Australia and a number of American and European centres and was included in the WHO agenda and on the homepage of the American Association of Blood Banks (AABB) in 2010 as an important principle for the improvement of transfusion safety.

Many POCTs can add up to a lot of blood taken

Unlike the EU-initiated Optimal Blood Use Project (EUOBUP), which aims to supply the right blood product to the right patient at the right time, PBM goes further – pursuing a preventive and corrective impact on those risk factors that usually lead to the need for transfusions. As Gudrun Hintereder MD, head of the central laboratory at the Wolfgang Goethe University Hospital in Frankfurt am Main, pointed out, PBM has been implemented in the USA for 20 years, but was only introduced in Germany in 2013.

The central laboratory provides significant support for this project to improve patient safety. Many point of care tests (POCT), plus routine and emergency laboratory examinations are carried out during a hospital stay, which, cumulatively, amount to a lot of blood. The frequency and amount of blood needed contribute significantly to the intensification or development of anaemia, an independent risk factor for increased rates of complications. Treatment of anaemia is often carried out with the help of banked blood transfusions; an expensive medical measure that can also cause numerous side effects.

The PBM programme at the Frankfurt University Hospital, a clinical, interdisciplinary project to improve care and safety, aims to preserve and enhance patients' own resources, and to reduce and prevent acquired and diagnostically induced anaemia and the adequate use of blood products.

Blood-saving measures

To ensure consistent process optimisation in the laboratory, the necessary minimum quantities required, whilst maintaining constant diagnostic quality are analysed. The volumes of existing blood collection tubes are reduced step by step. 'We also reduce the frequency blood is collected, although this means the patient must be well prepared for surgery, and we continuously check for possible anaemia. We have seen that we can make do with less, which has enabled us to save many litres of patient blood,' Hintereder explains.

The concept also includes blood-saving surgery. Perioperatively, as much blood as possible is collected and administered to the patient via cell-saver systems, which means that the use of banked blood products can be reduced. For some patients, a blood transfusion is the equivalent of organ transplantation, with all the associated risks such as infection or tolerance of the banked blood.

Anaemia diagnostics, smaller blood collection tubes, own-blood transfusion in the operating theatre – these are only three of more than 100 individual measures of patient blood management used by Frankfurt University Hospital, an international trailblazer in this field.

Gudrun Hintereder MD MBA has been head of the central laboratory at the Johann Wolfgang Goethe University Hospital in Frankfurt am Main since 2002 and is responsible for point of care test (POCT) analysis for the entire hospital. In 2010, she became an international assessor of the OLAS/ILNAS (Luxembourg) and the ILNAB (Ireland) for the accreditation of medical laboratories. Hintereder has worked on POCT and patient blood management since 2013.

Blood products also have a financial aspect. Since the willingness of the general population to donate blood has dropped, banked blood has become scarce and expensive. In Frankfurt, PBM has helped to save a tenth of the previous costs spent on blood products, which run into millions.

PBM results in lower morbidity and fewer strokes

The advantages for patients are even more significant. According to a German study, the number of patients with acute kidney failure has dropped considerably. In Western Australia, doctors in four large hospitals saw a lower morbidity rate and fewer strokes and heart attacks since PBM introduction.

All these advantages result from the consistent cooperation between clinicians and the central laboratory. Hintereder has observes that manufacturers are not geared up for blood management. 'Saving is not something the POCT equipment is set up for.' Therefore her appeal to the industry is: 'Make sure that you use less blood for analysis.'

One for all and ...

Continued from page 11

tor. Yet, because the accreditation requirement is mandatory, everyone knows that it is impossible not to go down this path.

'It helps to streamline and simplify the organisation of operations. And there were many follow-on benefits because it became clear that, for the personnel, work was easier in an accredited lab where the organisation is clear and consistent.

'For lab managers it became a tool for management-by-quality. In public hospitals, for example, there are very few tools for leveraging such a change, because it's not possible to create financial incentives for good performance. Here it became possible to manage by quality standards because it affects every sector, whether for investment decisions, or to bring together diverse groups around a project, because it becomes relevant and beneficial for patients,' he explained.

'In the end it remains difficult to say that patients receive better care from a hospital with an accredited laboratory operation than one that is not accredited. But,' Vaubourdolle concluded, 'if we keep patient access to quality care as our fundamental principle, with 100% accreditation we can show – we can prove – that access to care and the quality of that care is equal for everyone,'

IFCC experts unite to establish clear values

A new era for lab medicine

A new drive to increase the clinical effectiveness of laboratory medicine and take the discipline into a new era is being launched, Mark Nicholls reports

Coupled with steps to harmonise laboratory medicine services across Europe, a move to make lab medicine more clinically effective is being spearheaded by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

The latest position will be outlined at the EuroMedLab 2017 congress, booked for 11-15 June at the Megaron Athens International Conference Centre.

Former IFCC President Dr Graham Beastall will deliver a presentation looking at 'a proposed structure for defining, undertaking and reporting studies to assess the clinical effectiveness of laboratory medicine'. Presentations from other speakers aim to define and demonstrate clinical effectiveness in this field. 'Laboratory medicine results influence a high percentage of all clinical decisions,' Beastall confirmed during our European Hospital interview. However, this impact is diluted by variability in the services provided, the results obtained and the way in which those results are used.

Improving clinical effectiveness is not enough

'Consequently,' he pointed out, 'there is a global programme to harmonise the practice and delivery of laboratory medicine for the benefit of the patient.'

While the harmonisation programme has several dimensions - many of which are targeted at reducing the variability in results provided by different laboratories – Beastall maintains that this focus on improving analytical quality is not, by itself, sufficient to bring maximum benefit to patients. 'Improving the clinical effectiveness of laboratory medicine relies on the optimal delivery of the right test, to the right patient at the right time, coupled with a consistent interpretation of the results obtained, which are then translated into an evidence-based decision that will lead to the optimal clinical outcome for individual patients.'

He also pointed out that there are currently few clear examples of the link between the result of a laboratory medicine investigation and the optimal clinical outcome for patients. This may be down to various reasons, such as the 'weight of other clinical and diagnostic information and evidence that the physician has to consider'.

To address this, the approach in the new IFCC programme is to start with a single defined clinical outcome and then provide evidence of the impact that laboratory medicine results have in delivering that outcome.

Beastall's presentation aims to define appropriate clinical outcomes and give examples of how laboratory medicine impacts on them.

The IFCC proposed structure is constructed around a standard template for conducting clinical effectiveness studies with five defined stages: identify a specific clinical outcome; determine the impact that laboratory medicine should have on this outcome; gather evidence from the literature, or from a new study, to determine the actual impact of laboratory medicine data; prepare a report in a standard format leading to a recommendation on how to use laboratory medicine investigations to optimise clinical outcome; publish the report in a standard format creating a freely available, growing electronic library of studies linking clinical outcomes to laboratory medicine results.

Beastall suggests that a growing e-library of clinical effectiveness reports will provide a resource for laboratory medicine specialists to use in collaboration with their local physicians, and over time that will lead to greater harmonisation in the clinical application and use of laboratory medicine results.

To generate momentum in the project, an international cohort of laboratory medicine specialists willing to use the structure will need to be recruited, with IFCC co-ordinating studies and providing advice.

Entering a new era

'There is widespread recognition that laboratory medicine is entering a new era of impact on healthcare,' Beastall believes. 'To date, the focus has been on the growing availability of new tools and new technologies to improve the quality and expand the repertoire of investigation, especially at the molecular level.

'There needs to be a parallel drive to educate users of laboratory medicine services that the way in which new results may be used will be critical to the delivery of improved clinical outcomes.'

Such a move will enable pathologists and laboratory medicine specialists to provide a better service to users and patients. 'The broader impact of the initiative should be a gradual recognition by physicians, other healthcare professionals and patients of the importance of laboratory medicine,' he added. However, he stressed that success of the new initiative will depend on others accepting the invitation to embrace the proposed structure, perform clinical effectiveness studies and report them in a standard format.

Graham Beastall is a former President of the IFCC, having served as President from 2009-2014. Prior to 2009 he was Clinical Lead for a multi-site network Department of Clinical Biochemistry in Glasgow. He has published extensively on biochemical endocrinology and led IFCC projects to demonstrate the value of laboratory medicine in healthcare and to promote the need for increasing clinical effectiveness. Beastall was formerly President of the Association for Clinical Biochemistry (ACB) and Vice President of the Royal College of Pathologists (RCPath) in the United Kingdom.

* The IFCC Symposium: 'Increasing clinical effectiveness in laboratory medicine'. 13 June. 10.30am-12.30pm Skalkotas Hall, Megaron Athens Centre, .

Hindered by proteins and the human proteome complexity

Strategies to advance cancer biomarkers

Report: Mark Nicholls

Cancer biomarker testing represents an important element of the clinical biochemistry service, yet progress in this area in the last two decades has been slow.

With no major new serum cancer biomarkers introduced into clinical use within the last 10 years - despite advances in various omics technologies - experts are continuing to work hard to unlock the technological potential to advance the diagnostic and treatment options available to patients.

Strategies to discover and validate novel biomarkers

A symposium on advances in biomarker discovery, will examine strategies for discovering and validating novel cancer biomarkers by using a combination of omics technologies, during the EuroMedLab 2017 congress in Athens this June.*

Among the speakers will be Dr Vathany Kulasingam, from the University Health Network in Toronto, Canada, who will focus on mass spectrometry as a tool for cancer biomarker discovery. 'Mass spectrometry,' she pointed out, 'is a powerful analytical tool and the use of this technology for this application is not novel. However, very few serum cancer markers have reached the patient. For what reason? What are the hurdles?'

The huge complexity of the human proteome

Points she will focus on are the challenges associated with biomarker discovery, including the complexity of the proteins and human proteome, the importance of having a good biorepository and a good study design to avoid bias. 'It's important to use this technology to help us understand the biology of the disease,' she added. 'We must have a fundamental initial question to ask and we have to understand the disease and its biology. We can use mass spectrometry to help us understand that and then refine our questions better.'

However, a major challenge has arisen due to the under-estimation of the human proteome complexity.

While there are ~20,000 protein-coding genes, Kulasingam said, the human protein is estimated to have 500,000-1,000,000 proteo forms because of single nucleotide variants, alternative splicing and post-translational modifications.

'Mass spectrometry can provide both structural as well as quantitative information, that's the key. Will this yield novel biomarkers? I'm not sure yet because we do not have such data, but I think this is one avenue to explore.

'We now have a strong understanding of the importance of good study design, appreciating pre-analytical considerations, asking the correct biological questions, and we understand the importance of having good biorepositories.'

That need for good clinical information and samples is now more clearly recognised for biomarker discovery and validation, particularly after work carried out using more conveniently accessible samples had unintentionally led to false discoveries.

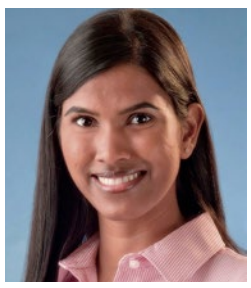
No major discovery since the '80s

With limited discoveries in serum biomarkers, with nothing major since the 1980s, Kulasingam believes the way is now clearer to advance cancer biomarker discovery but adds, 'We have come a long way but I think we still have a while to go.'

This symposium in Athens will offer participants a greater understanding of how systems biology can contribute to new biomarker discovery while highlighting the difficulties associated with cancer biomarker discovery and why many promising cancer biomarkers fail in the clinic.

Also speaking at the session is Henry Rodriguez, Director of the Office of Cancer Clinical Proteomics Research at the National Cancer Institute at NIH, focusing on 'Proteogenomic analysis of cancer: New opportunities in cancer biology and precision medicine', and Professor Catherine Alix-Panabières from the Faculty of Medicine at the University of Montpellier, on 'Gfr and drug dosage adaptation: are we still in the mist?'

* 12 June. 10.30am-12.30pm. 'Advances in cancer biomarker discovery' symposium. Lambrakis Hall, Megaron Athens International Conference Centre.



Vathany Kulasingam is a clinical biochemist at the University Health Network in Toronto, an Assistant Professor at the Faculty of Medicine, University of Toronto and Fellow of the Canadian Academy of Clinical Biochemistry. Her current interests include novel tumour biomarker discovery and application of proteomics to clinical practice.

New model to aid antibiotic resistance studies

Scientists in the UK have developed a new model that will help to advance the study of resistance to antibiotics.

Research presented at the recent European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) demonstrated that resistance to carbapenem (and other) antibiotics can be studied using a laboratory antibiotic resistance model that accurately simulates conditions in the large intestine.

The research was led by Professor Mark Wilcox, Head of Microbiology and Academic Lead of Pathology at the Leeds Teaching Hospitals (LTHT) who explained that the model shows that rapid transfer of genes that code for the enzymes responsible for carbapenem resistance can occur.

A similar model has been used in Leeds for the past 15 years to predict the risk of Clostridium difficile infection (CDI) and the effectiveness of new treatment options, resulting in some 30 publications to date.

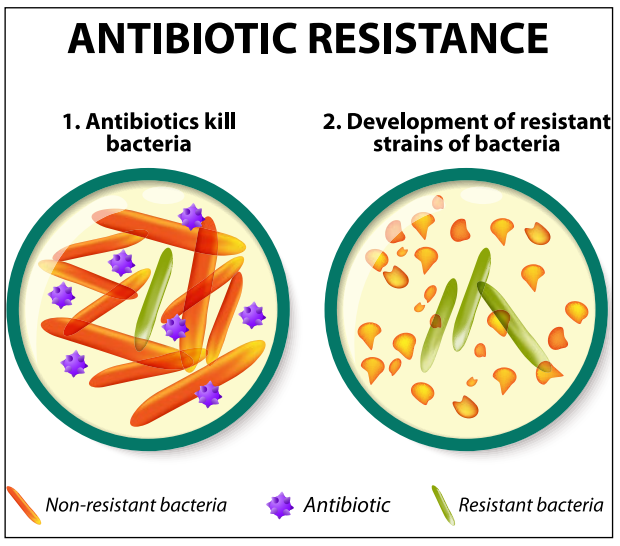
The study showed that resistance levels in the pathogens most commonly associated with healthcare associated infections (Enterobacteriaceae and Pseudomonas aeruginosa) is higher in the ICU setting than in non-ICU settings – a concern for hospital managers and clinicians because ICU patients are typically more severely ill, more likely to have poor outcomes, and are more costly to manage.

'The new antibiotic resistance gut model offers the opportunity to better understand which conditions (e.g. particular antibiotics) are more likely to be associated with the emergence and spread of carbapenem resistance,' added Wilcox, who is the Lead on Clostridium difficile for Public Health England (PHE). 'Also, it's possible using this approach to determine whether antibiotics under development - including for the treatment of carbapenem resistant infections - are associated with a low or high chance of emergence of resistance.'

Carbapenems are antibiotics used to treat infections known or suspected to be caused by multidrug-resistant (MDR) bacteria and primarily on hospital patients. The issue of nosocomial antibiotic resistance is of a major concern globally. 'This is an extremely serious threat, given the lack of suitable alternative treatment options and rapid spread of resistance in some settings,' he pointed out.

In separate research, an international consensus report highlighting the need for improved management of Clostridium difficile infection (CDI) in inflammatory bowel disease (IBD) patients (authored by Wilcox) was presented at ECCMID.

'The international consensus report highlights that more information is needed to optimise the diagnosis and treatment of CDI in patients with IBD,' he said. 'We know that CDI has important consequences for patients and healthcare systems, including excess morbidity, mortality and length of hospitalisation. These consequences are most pronounced in vulnerable patients, including those with inflammatory bowel disease.' *(MN)*



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Mark Wilcox is a Consultant Microbiologist, Head of Microbiology and Academic Lead of Pathology at the Leeds Teaching Hospitals (LTHT), Professor of Medical Microbiology at the University of Leeds (Leeds Institute of Molecular Medicine), and the Lead on Clostridium difficile for Public Health England (PHE). He is also Deputy Chair of the UK Department of Health's Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) Committee and an advisor to the Department of Health in England on healthcare associated infections (HCAIs). Additional roles include being a member of UK, European and USA working groups on CDI. His research focuses on HCAI, in particular CDI, staphylococcal infection, and the clinical development of new antimicrobial agents.

Wanted: an automated clinical LC-MS/MS analyser with broad, expandable testing menu

Liquid chromatography tandem

Combining the physical separation power of liquid chromatography with the mass analysis capability of mass spectrometry – i.e. liquid chromatography tandem mass spectrometry (LC-MS/MS) – enables accurate, sensitive and selective separation, detection and identification of molecules in complex mixtures such as blood, serum and urine.

Senior biomedical scientists from the Cardiff and Vale University Health Board, United Kingdom, consider LC-MS/MS an important tool in running powerful diagnostic analyses across a range of applications, including endocrinology, toxicology and metabolic screening. However, like many other clinical diagnostic laboratories around the world, they admit they do not use the technology to its full potential.

Here, Gareth Jones, Luke Griffiths and Paul Bramhall, members of the Cardiff team, describe obstacles that prevent wider adoption of the technology and share their belief that a standardised and automated clinical LC-MS/MS analyser with a broad and expandable testing menu may overcome the challenges of current methods. This could establish LC-MS/MS as the technology of choice for clinical diagnostic testing.

The challenges

It is well recognised that current LC-MS/MS systems have a limited testing menu. This makes it time consuming for laboratory professionals to develop, review and validate new assays that would allow them to run a wider variety of tests. Additionally, analyses performed using current LC-MS/MS methods involve several complex manual steps, including sample acquisition and preparation.

Complexity is further increased because, in many cases, multiple separate tests must be performed to generate a single analytical result, leading to considerable time and cost inefficiencies. 'Using our current LC-MS/MS systems,' Gareth Jones explains, 'we have to spend up to four days undertaking three different tests to obtain a full steroid profile. It would be much more cost-effective if these tests could be run simultaneously on one instrument.'

Another key challenge is the lack of laboratory staff sufficiently trained to use LC-MS/MS technology to its full potential. 'Due to the overly technical nature of our current LC-MS/MS systems, only six of our team of 60 biomedical scientists have the specialist skills necessary to run them,' Jones adds. 'This poses a particular problem for our out-of-hours service.'

For all these reasons, automated immunoassays have remained the preferred method within clinical diagnostic laboratories for many years. Yet, modern LC-MS/MS techniques offer some considerable benefits.

The analytical power of LC-MS/MS

For certain analytes, immunoassays can be subject to interferences, limiting their specificity and reducing the quality of results compared to LC-MS/MS. In addition, immunoassay-based methods can be very time consuming. 'Some tests take only two minutes using LC-MS/MS compared to the 40 minutes it takes to use an immunoassay-based test,' Luke Griffiths points out.

A further disadvantage of immunoassay-based tests is that they are developed in kit form and require FDA approval – a procedure that may take a few years to complete. 'There have been cases where we have waited two years for an immunoassay kit to become available. Alternatively, after completing validation and verification on an LC-MS/MS system you could have run a test immediately,' Paul Bramhall explains.

As always, cost is an important consideration in evaluating different analytical methods. 'LC-MS/MS does require a greater outlay upfront,'

Significantly shorter therapy durations may be sufficient

Killer bugs put on the critical list

While new agents to fight virulent pathogens are in the pipeline, a new study pinpoints where a recent addition is already being applied in the clinic, John Brosky reports

Bacterial resistance to antibiotic therapies is a global crisis that recently prompted the World Health Organisation (WHO) to publish its first ever list of pathogens considered to be a priority for the threat they pose to human health.

Among the 12 pathogens singled out, a virulent bacterium named Pseudomonas Aeruginosa was among three considered to be critical in terms of need for new therapies to combat this killer.

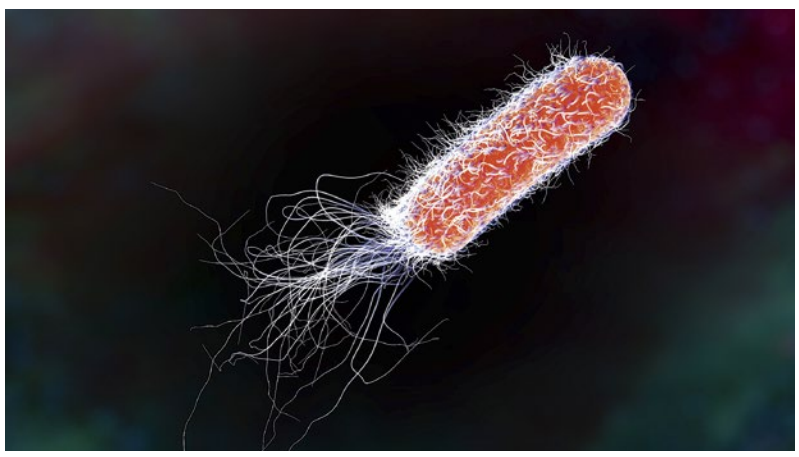
A new strategy to fight these often fatal infections has emerged in the form of combination therapies, where a parent drug capable of neutralising the harmful bacteria is paired with an agent that can either protect the active molecule from bacterial resistance tricks, or else can facilitate the penetration of the second agent into the bacterial cell so the neutralising molecule can go to work.

Many of these promising new agents are still in pre-clinical stages, and some are moving through clinical trials. In other words, few are ready and approved for prime time use in intensive care units (ICUs) where patients are suffering.

A clinical pharmacist specialising in infectious diseases at Sinai-Grace Hospital in Detroit, Michigan, Jason Pogue, Pharm.D, set out to learn where one of the more promising newer agents is actually being used in the clinic and the effectiveness of its use.

Randomised controlled trials of the combination of the parent drug ceftolozane with an inhibitor agent tazobactam, in target populations, will ultimately answer the question of efficacy for clinicians, he said. Ahead of that key piece of evidence, Pogue said a description of real-world utilisation is helpful to describe for clinicians what has been done in clinical practice as a supplement to clinical trial data.

At the 2017 European Congress of Clinical Microbiology and Infectious Diseases, held in Vienna this April, Pogue presented a poster including 293 patients receiving the ceftolozane-tazobactam therapy who were identified through an electronic research database of 315 hospitals in the United States maintained by the Becton Dickinson Company. The study was supported by Merck & Co., which manufactures the ceftolozane-tazobactam combination therapy under the brand name Zerbaxa.



Pseudomonal infections are complicated and can be life threatening. The common pathogen Pseudomonas Aeruginosa, for example, frequently causes nosocomial infections such as pneumonia, urinary tract infections and bacteremia

Among the 293 patients there were 314 treatments, most often started in the ICU and most often to treat respiratory tract infections. The most common pathogen was Pseudomonas Aeruginosa, which was isolated in 241 cases or 77% of the combination courses of treatment.

The conclusion for the study remains necessarily inconclusive as to the effectiveness of treatment, Pogue said. Instead the data is descriptive of how the therapy is being applied, particularly as these data show the agent is being used outside of the labelled indication in nearly half the cases.

In a next step, the pharmacist said, the study lends itself to a comparison to patient populations who received other therapies for the same type of conditions identified in the ceftolozane-tazobactam study, bringing clinicians closer to the efficacy question ahead of the results from clinical trials, and as a complement to those trial results once published.

'As these data show, the primary use of ceftolozane/tazobactam in the clinic is for respiratory tract infections with Pseudomonas Aeruginosa. However, the published evidence to support this is very limited. Approval of this combination was granted on the basis of efficacy against specific disease states (urinary tract infections and intra abdominal infections), not against a pathogen. Yet, because thankfully these resistant organisms are relatively rare, there is unfortunately a lower likelihood they will be encountered in a registry trial for drug approval. The clinical concern for drug resistant P. aeruginosa is in the respiratory tract where, as stated, data are currently lacking,' he said.

'What we found through our analysis is that the primary use of ceftolozane/tazobactam appears to be for Pseudomonas Aeruginosa in patients with nosocomial pneumonia and, while the combination drug is not approved for that indication,

Dr Jason Pogue is an infectious diseases clinical pharmacist at Sinai-Grace Hospital in Detroit, MI. He also serves as an assistant clinical professor of medicine at the Wayne State University School of Medicine. He received a bachelor degree in Chemistry from Gannon University before obtaining his doctor of pharmacy degree from the University of Pittsburgh. He then completed a PGY-1 residency at the University of Pittsburgh Medical Centre, after which he left Pennsylvania for Michigan to obtain his PGY-2 ID training at the University of Michigan Health Systems. His research interests focus on epidemiology and treatment of multi-drug resistant Gram-negative organisms and antimicrobial stewardship, and he has co-authored over 70 peer reviewed articles, 100 abstracts at national and international meetings and multiple book chapters in these areas. Pogue was recently invited to become an advisor for USCAST, an organisation that aims to standardise antimicrobial susceptibility breakpoints in the USA.

mass analysis

says Jones. 'However, beyond this initial investment, the operating costs are much lower than immunoassay-based tests.'

Consequently, laboratories could significantly benefit from using LC-MS/MS systems rather than immunoassays, as they would be able to generate more specific results in a more time- and cost-efficient manner.

The solution

The Cardiff team is confident the solution lies with the creation of a standardised, automated clinical LC-MS/MS analyser with a broad and expandable testing menu. Such a system would enable laboratories to perform a growing number of tests, and enhance result accuracy and reliability – thus improving patient care.

An advanced analyser would also increase the laboratory's ability to develop and validate new assays, while also enabling their standardisation across different laboratories. 'Regulatory certification has become essential. A ready-made system with FDA approval and CE marked with traceability would benefit any laboratory introducing LC-MS/MS,' Jones believes.

In addition, an automated LC-MS/MS system would be as simple and easy to set up and use, as modern automated immunoassay-based methods, reducing the need for personnel with specialist knowledge of the technology. Laboratories would thus be able to ensure the best possible service is offered to healthcare providers at all times, even during the out-of-hours service. Considerable time would also be freed up for the more experienced scientists to invest in cutting-edge research and development, and troubleshooting of results.

A further important benefit of such a sophisticated system would be reducing the number of manual steps, which would lead to considerably improved turnaround times and reduced chance of human error. Clinical and biomedical scientists would also be able to routinely perform multiple tests and develop assays on a single instrument to improve efficiency and increase productivity.

'Our major driving force has always been quality – and we view LC-MS/MS systems as the gold standard,' says Bramhall. 'However, the challenge is how we optimise the quality of testing while maintaining time and cost efficiencies,' Griffiths adds.

A dedicated, automated clinical LC-MS/MS analyser with a broad and expandable testing menu has the potential to do just that.

* Article source: Sarah Robinson, PhD, Market Development Specialist, Thermo Fisher Scientific

though a trial has been started, in the real world of clinical practice the treatment is being used in the ICU. Again, the point is not to say this combination works but instead to describe where clinicians have utilised it,' Pogue said.

Awaiting wider approval for new agents against the pathogens identified by the WHO, Pogue said clinicians apply different strategies to preserve the effectiveness of the antibiotics that are available.

Pogue is an advocate of an approach called stewardship that centres on reserving antibiotics so that the pathogen does not learn to resist them. The four tenets of antibiotic stewardship consist of giving patients the right drug in the right dose with the right delivery method and, according to Pogue, most importantly, for the right duration of treatment, neither too short nor too long.

'For most diseases caused by infections there is good evidence that significantly shorter therapy durations are probably sufficient. Right now we are working hard to find that sweet spot for optimal treatment, finding the low end of the duration that matches with efficacy,' he said.

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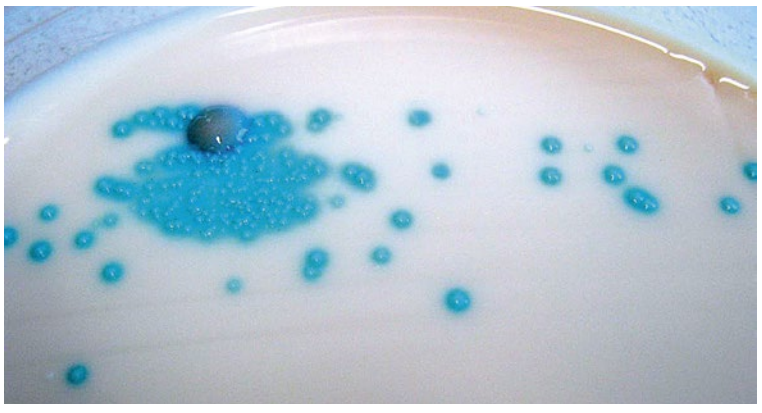
95 percent of hospital patients move through without infection

Successful antibiotic stewardship programmes

Today's dilemma for hospitals and institutions are increasingly multi-resistant bacteria and decreasingly effective antibiotics to beat them. New substances to fight pathogens are not on the horizon. What can be done? Professor Constanze Wendt, microbiology and infection biology specialist at MVZ Labor Dr. Limbach & Kollegen GbR, in Heidelberg, Germany, describes current anti-infection strategies in German hospitals.



Antibiotic stewardship in clinical routine - The German guideline to ensure rational use of antibiotics in a hospital, drafted in 2013, led to so-called antibiotic stewardship programmes being implemented in most hospitals.

These programmes aim to optimise the use of antibiotics by appropriate selection, dosage, application and length of therapy, so as to slow down resistance development while maintaining best outcomes. For this purpose interdisciplinary hospital task forces have been established to collect and analyse internal data. They look at which antibiotics have been subscribed in what doses; which type of resistances occurs most frequently and which antibiotics can be used against what types of pathogens in a targeted fashion.

Based on answers to those questions the task force can draft tailor-made therapy guidelines, taking into account the facility's complexity, clinical disciplines and patient population. The results are promising. Even though a comprehensive evaluation still needs to be done, individual hospitals could reduce the use of antibiotics.

An interdisciplinary approach - The German guideline mandates specific structures and qualifications to implement the antibiotic stewardship programmes. In addition to microbiologists, infectiologists, hospital hygiene specialists and clinicians, each task force needs an antibiotic expert. The curriculum-based training is certified. 'These preconditions demanded by the guideline need to be met before the task force can go ahead,' Wendt explains.

The professional associations, various medical associations and the German Society are offering this training programme for Hospital Hygiene.

Targeted therapy - Standards developed in individual hospitals allow the physicians to target the therapies more precisely. Whereas patients frequently had received a broad-spectrum antibiotic, today the approach is far more differentiated. The data collected in-house show which bacteria are to be expected with which infection and which bacteria have turned out to be resistant. The selection of a medication is as 'narrow' as possible and as broad as necessary to provide the patient with an ideal therapy.

Since samples are analysed in the lab to identify the bacterium, therapy can be adjusted if necessary after two or three days.

Hygiene - Strategies to combat bacteria include preventive hygiene measures. To avoid contagion, it is recommended that high-risk patients be washed with an antiseptic. Initial evaluations of this measure are underway but the current data do not yet warrant overall implementation. 'Theoretically we all know what to do in terms of hygiene. Nevertheless, we are working on spreading the hygiene culture. While this sounds trivial it is in fact the most difficult task,' Wendt points out.

With a Master of Science degree in Preventive Medicine and Environmental Health **Professor Constanze Wendt MD** is also a specialist physician for hygiene and environmental medicine as well as microbiology and infection epidemiology. As head of the hygiene department at Limbach Gruppe SE, MVZ Labor D. Limbach & Kollegen, in Heidelberg, Germany, with her team she advises hospitals, from primary to maximum care, as well as outpatient surgery centres, dialysis centres and rehabilitation facilities on all hygiene management issues.

In general, hospital hygiene procedures are complied with; nevertheless, in times of staff shortages and extreme workload they may tend to be watered down. Thus multimodal training approaches are required that continue to drive home the issue and trigger sustainable behavioural changes.

This involves presentations such as posters, role models, observation and feedback on hygiene behaviour as well as compliance checks – a long-term task, no doubt, but one with high chances for success as Wendt concludes: 'With an infection rate of three to five percent we could increase safety to a very high level, since this translates to 95 percent of patients moving through the hospital without acquiring an infection.'

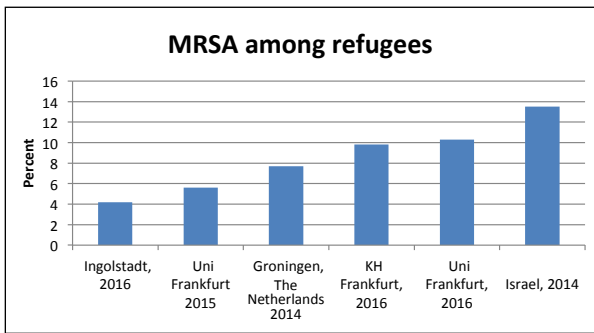
Research lags behind – For many years, antibiotics have been a very effective and fast therapy. Today, however, bacteria are developing resistance faster than research teams can develop new antibiotics. The situation is spiralling beyond control. Moreover, antibiotics launched in the past ten to twenty years contain hardly any truly innovative active ingredients. They were mostly modifications of existing drugs rather than entirely new ones – consequently the bacteria 'knew' them and could develop resistance even faster.

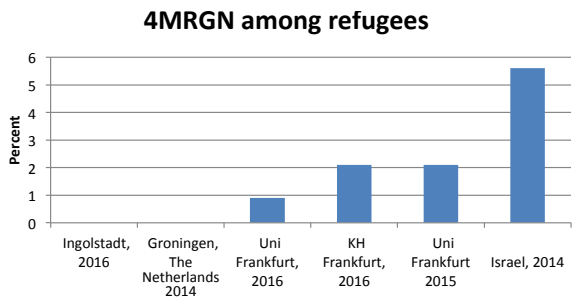
Whilst many reasons exist for the lack of innovation, it is undisputed that the development of new drugs is time-consuming, fraught with setbacks and thus expensive. Professor Constanze Wendt warns: 'We're running out of time. There are only a few antibiotics left that we can use. It is crucial for us to develop new strategies.'

Call to screen refugees for MRSA and MDGRO upon hospital admission

Screening, isolation, hygiene equal money well spent

Comprehensive examinations of 143 refugee patients* hailing mostly from Afghanistan and Syria, which were conducted between June and December 2015, showed a high prevalence of MRSA, ESBL and MDRGN upon hospital admission. The figures exceed not only those of the general population but, alarmingly, also those found in high-risk groups, such as residents of nursing homes or home care service patients. Professor Ursel Heudorf of the Department of Infectiology and Hygiene at the Public Health Office in Frankfurt, Germany, is therefore demanding general screening of refugee patients upon hospital admission.





Data speak the truth - In the population at large, MRSA rates are below one percent. Among groups at risk, such as nursing home residents, it is six to nine percent. However, among the refugee patients examined in the Rhine-Main region 9.8 percent carried MRSA. -Found to be present in approximately eight percent of the general population, these organisms were detected in risk groups between 7.5 percent (dialysis patients), 14 percent (patients of home care services) and 18 to 27 percent (nursing home residents).

During the above-mentioned study the organisms were present in 23 percent of the refugee patients, with 1.8 percent carrying MDRGN bacteria, resistant to four classes of antibiotics. Thus, refugee patients present a more severe health threat for themselves and others than the typical at-risk groups in Germany, even though the patients were primarily young and presumably without an extended history of hospital stays. 'The result was surprising and warrants a re-evaluation of this patient group,' says Professor Ursel Heudorf, Public Health Physician and Director of the Hygiene Department at the Public Health Office in Frankfurt/Main, Germany. While elderly people stay in hospital frequently and are treated with antibiotics, they have always been considered an at-risk group and undergo suitable hygiene procedures, refugee patients only now have been understood to be on a similar risk level and require corresponding hygiene measures.

Questioning why

Why such a large prevalence of MDRO? Heudorf assumes one reason to be 'improper antibiotics management in the countries of origin of the refugees'. The lack of product quality assurance in the countries of origin, where antibiotics are frequently sold over the counter and might contain a lower concentration of active ingredients, might be one factor; costs might be a second one. Since the pharmaceuticals are freely available on the market they may be taken as long as they can be afforded. This may lead to antibiotics therapy being stopped prematurely since the patients subjectively feel better. 'There are several conditions that promote resistance,' Heudorf concludes.

Evidence-based recommendation

Therefore, she considers it 'important to screen all refugee patients upon hospital admission'. Even the Robert Koch Institute (RKI), which previously recommended tests only if warranted by the individual patient's medical history, now also supports screening for MRSA and 4MDGRN upon hospital admission.

Medical history-based tests are difficult to implement in practice, as Heudorf points out: 'Too complicated, too error-prone. Due to language problems on both sides, the validity of the information provided is questionable.'

Thus, systematic screening and initiation of hygiene measures should be performed regardless of the information provided by refugee patients during anamnesis. Heudorf is well-equipped to master future challenges. 'Our study in the Rhine-Main area was prompted by the lack of knowledge on our new and relevant patient group – refugees. The results allow us to design an evidence-based approach.'

Preventive isolation

Depending on the procedure, each test will cost between three and 50 euros. The gold standard remains the culture on a petri dish. PCR is faster, but provides rather too many false positives.

Heudorf recommends preventive isolation even before the test results are available, to be able to decide on the next steps based on results. Isolation, however, means more costs both in terms of time and human resources, for example changing times for staff.

Isolation also requires more space, since only one bed can be used per room. However, financial considerations notwithstanding, Heudorf is convinced that 'if an outbreak of multi-resistant pathogens is to be prevented in a hospital, in the end money spent on screening, isolation and hygiene is always money well spent.'

Professor Ursel Heudorf MD, Public Health Physician and Deputy Director and Director of the Hygiene Department at the Public Health Office in Frankfurt/Main, Germany, is an expert in hygiene in medical and community facilities with a focus on multi-resistant organisms. She initiated and today heads the MDRO (Multi Drug Resistant Organism) Network Rhine-Main, which offers a wide range of services for the general public and an expert audience – such as studies on MDRO prevalence in non-acute clinical settings. The network conducted the largest multi-centre study on MDRO among refugee patients to date (all studies and further information available on www.mre-rhein-main.de).

Significantly shorter therapy durations may be sufficient

Dangerous travel companions

Trips around the globe, healthcare tourism, migration; we are mobile – and so are bacteria. Particularly dreaded are multi-drug resistant bacteria that 'hop' on their host during a hospital stay and are carried across the border. At MEDICA 2017 Labmed Forum Dr Andreas Ambrosch, Head of the Central Lab at Krankenhaus Barmherzige Brüder in Regensburg, Germany, will discuss these unwelcome international travel companions.

Scientists in Scandinavia, the Netherlands and Germany have conducted comprehensive research on the link between increasing human mobility and the spread of bacterial resistance. Several studies with healthy volunteer subjects showed that travellers who were initially pathogen-negative carried multidrug-resistant bacteria upon their return, in most cases ESBL-producing E. coli or Klebsiella spp. type CTX-M (ESBL = extended spectrum beta-lactamase).

High-risk trips involved India (80%), followed by the rest of Asia (slightly below 50%), the Middle East and Southern Europe (approx. 15%). These and other studies found traveller's diarrhoea and antibiotics therapies during the trip to be independent risk factors.

Average length of colonisation with ESBL-producing bacteria was 30 days; in 10% of the cases, however, the pathogen continued to be present after one year. Even family members who had not travelled were infected (12%).

Healthcare tourism

According to the general, as well as the healthcare, media, in Germany infections with pan-resistant bacteria (with colistin the only therapy option left) are frequently traced back to patients who received emergency care in a foreign hospital. Thus, the first European patient to be diagnosed with carbapenemase type NDM-1 (New Delhi Metallo-beta-lactamase-1) was a Swede who had undergone treatment in New Delhi, India.

Patient Zero, in a major outbreak of KPC-2 carbapenemase-producing Klebsiella at a German university hospital, had previously been treated in a Greek hospital. It took almost three years to end the outbreak: more than a hundred patients had been colonised and infected, at least 15 died of the infection.

A recently published study on the incidences of multi-drug resistant bacteria in foreign hospital patients in Frankfurt reported highly resistant carbapenemase-producing bacteria, particularly Acinetobacter baumannii, in 5% of the cases. The last two patients in our facility in Regensburg found to carry Acinetobacter baumannii resp. KPC-2 Klebsiella classified as 4MDRGN (multi-drug resistant Gram-negative bacteria resistant to 4 classes of antibiotics), were previously treated in a hospital in Hungary (relating to Thailand).

Immigrant population

The high number of immigrants currently entering Germany raises public concern, politically as well as in terms of healthcare. Medically speaking, this concern is not entirely unfounded: a recent study on the prevalence of hygiene-relevant pathogens in immigrants at an admission centre in the Saarland showed 40% of the people tested to carry MDRGN resistant to two or three classes of antibiotics (for comparison: 5-10% – regional differences – among patients in German hospitals). Most frequently, E. coli or Klebsiella spp. were identified.

A study testing unaccompanied minors in Frankfurt, 70% of whom hailed from Afghanistan, showed very similar results: in 34% of people tested, ESBL-producing bacteria were detected, 8% of which were categorised as 3MDRGN (incl. quinolone resistance). No pan-resistant species (4MDRGN) were found.

An updated statement by Robert Koch Institute now recommends screening of refugees upon hospital admission due to the high prevalence of multi-drug resistant bacteria in some countries of ori-

Conflicting theories and not enough research

Hand washing: in hot or cold water?

Report: Brenda Marsh

'The literature on hand washing, while extensive, often contains conflicting data, and key variables are only superficially studied, or not studied at all. Some hand washing recommendations are made without scientific support, and agreement between recommendations is limited,' explained Professor Donald W Schaffner at Rutgers University, New Jersey, USA, who has led a team of researchers to clarify this underdetermined situation. Specifically, they set out to investigate the influence of key variables, such as soap volume, lather time, water temperature and product formulation on hand washing efficacy.

One of their most interesting findings concerns water temperature, a subject on which the USA"s Food and Drug Administration (FDA) stipulates that warm water, rather than cold water, is more effective to remove germs during handwashing. The FDA advises caterers, for example, to adhere to a water temperature of 40° C, plus or minus 2 degrees (100-108°F). The idea is that hot water lathers up soap and therefore ensures spread throughout hands.

However, The USA's Centre for Disease Control and Prevention (CDC Guideline for Hand Hygiene in Healthcare Settings) recommends:

- When cleaning your hands with soap and water, wet your hands first with water, apply the amount of product recommended by the manufacturer to your hands, and rub your hands together vigorously for at least 15 seconds, covering all surfaces of the hands and fingers.
- Rinse your hands with water and use disposable towels to dry. Use towel to turn off the faucet.
- Avoid using hot water, to prevent drying of skin.
- Other entities have recommended that cleaning your hands with soap and water should take around 20 seconds.
- Either time is acceptable. The focus should be on cleaning your hands at the right times.

In England, from 1998-2000, a nurse-led multi-professional and specialist clinicians research team, commissioned by the Department of Health, produced the national evidence-based guidelines for preventing healthcare-associated infections (HCAI) in National Health Service (NHS).

The guideline: Effective handwashing technique involves three stages – preparation, washing and rinsing, and drying.

- Preparation: wet hands under tepid running water before applying the recommended amount of liquid soap or an antimicrobial preparation.
- Washing: the hand wash solution must come into contact with all of the surfaces of the hand. The hands should be rubbed together vigorously for a minimum of 10-15 seconds, paying particular attention to the tips of the fingers, the thumbs and the areas between the fingers. Hands should be rinsed thoroughly.
- Drying: use good-quality paper towels to dry the hands thoroughly.

The same rationale is not dominant in many, or most, European countries – though belief and practice can be personal.

In the new Rutgers University research (pub: Journal of Food Protection. May 2017):

'Quantifying the Effects of Water Temperature, Soap Volume, Lather Time, and Antimicrobial Soap as Variables in the Removal of Escherichia coli ATCC 11229 from Hands', bland non-antimicrobial soap was lathered up for 5 seconds using 38°C (100°F) water temperature.

The microorganism used was Escherichia coli, as cited in the research title. 10 men and 10 women took part in the research over a six-month period, to measure the effects of hot and cold water and the elements also listed in the title.

The devised test was replicated 20 times, when the volunteers washed their hands in water that was 16°C, 26°C, or 38°C.

Different amounts of soap were used: 0.5 millilitres, one millilitre, or two millilitres.

Antimicrobial soap (1% chloroxylenol) did not prove particularly more effective than regular soap in removing the E. coli within the various tests. In one aspect, however, lathering time notably improved efficacy.

Water temperature had no significant effect on bacteria reduction. Whether 38°C or 16°C, the team detected no difference in bacteria reduction.

The study also showed that washing hands for as little as 10 seconds proved effective against germs.

'People need to feel comfortable when they are washing their hands, but as far as effectiveness, this study shows us that the temperature of the water used didn't matter,' Schaffner concludes. 'There should be a [US] policy change. Instead of having a temperature requirement, the policy should only say that comfortable, or warm, water needs to be delivered. We are wasting energy to heat water to a level that is not necessary,' he added, suggesting that the policy should advise the use of 'comfortable, or warm water'.

The researchers recommend more studies to determine how much soap and what type is most effective to remove pathogens.

gin. However, people who underwent treatment in a foreign hospital seem to pose the greater risk, since the risk of colonisation with pan-resistant bacteria is higher in these facilities. Proactive and preventive isolation, until screening results are available, seems advisable.

Travellers should be aware that, depending on their destination, colonisation with multi-drug resistant bacteria might be an unwelcome souvenir. Any physician who diagnoses such colonisation should expand the anamnesis or, if in a hospital, refer to screening. However: there is no reason to panic. Colonisation with multi-drug resistant bacteria is, in general, without symptoms. Contamination and spreading of the bacteria is most effectively prevented by adequate hand hygiene.

* The article was first published by Trillium Diagnostik 2017; 15(1):56

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