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EUROPEAN HOSPITAL

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Brexit: Uncertainty in every question

Will existing healthcare standards remain or follow those of the USA?

The British decision to leave the European Union was and still is constantly discussed. Thinking about the consequences leaves more open questions than answers. 'Unsurprisingly, most informed commentators use the word "delusional" rather a lot,' says Martin McKee, Professor of European Public Health at London School of Tropical Hygiene and Medicine.

At the European Health Forum in Gastein (EHFG) he discussed the current situation with Professor Helmut Brand, president of EHFG, and Jean Monnet, Professor of European Public Health and head of the Department of International Health at Maastricht University. Both agree: In many areas, the NHS depends on EU citizens and also the challenges that now must be faced go much deeper than anyone who voted for Brexit ever thought.


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Many and various scenarios have been discussed in recent months. Several steps are already undertaken. How much time might Brexit take?

McKee: 'Much longer than two years to be concluded, if Brexit ever is. The two years specified in Article 50 only cover agreeing how the UK might exit. We should recall that Greenland, with only 50,000 people and one major issue – fishing – to discuss, took three years.'

Brand: 'I'd like to add that the European Healthcare System will not be very much affected by Brexit, but the UK will be. There are fewer British medics working in the EU than EU medics working in the UK. These, however, will be affected. I know a lot of post-graduates who have problems with the renewal of their expiring contracts and who do not know whether they can stay in the UK, or not. I recognise a big uncertainty, both on the official side and in the Healthcare System, at the moment.'

What is the next step and challenge?

McKee: 'There are two major challenges facing the world. The first, and most urgent, is concerted agreement on climate change. We now do have the Paris Agreement on how to proceed. The challenge is to make it happen. The second is to develop concerted plans to implement the Sustainable Development Goals (SDGs). These provide a solid basis for progress for our planet, but will require the world's nations to match their words with resources. In the rest of the world, there are many important issues to resolve, among them the implementation of the SDGs. They include the need to achieve peace in the Middle East, which would do much to stem the flow of refugees that is placing so much pressure on countries neighbouring Iraq and Syria and, to a much lesser extent, Europe, as well as defusing tensions in the South China Sea.'

Everyone is awaiting outcomes relating to the results of the US Presidential and senate and house elections, McKee added.

'In the UK, government is largely in a state of paralysis, with most departments being urged to implement Brexit, but no idea about either what it means, except that "Brexit means Brexit", or how to begin. We can anticipate many years

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The 1st ETIM Congress – February 2017

Emerging medical technologies

Artificial intelligence and bio-printing will be the central theme of an ETIM 2017 congress,, which will be held at the University Hospital, Essen, Germany, on 10-11 February 2017.

Congress chairmen, Professor Michael Forsting, Head of the Department of Radiology and Neuroradiology, and Professor Jochen Werner, Medical Director and Chief Executive Officer, University Hospital of Essen, are inviting clinicians, computer scientists, engineers, researchers, healthcare providers, legislators and other involved disciplines to this first interdisciplinary conference. 'Further acceleration of medical innovation by upcoming technologies such as artificial intelligence and bio-printing can be safely predicted,' Forsting points out. Technologies such as individual genome sequencing, high-performance multiparametric imaging, or wearable medical devices, generate exponentially growing datasets, while contemporary data-mining techniques allow the extraction of large amounts of valuable data from existing archives of unstructured medical data. Of this he is convinced: 'These offer the chance for highly specific clinical decision-making and personalised precision medicine.'

Congress chairs: Michael Forsting (left) and Jochen Werner

Details: https://etim.uk-essen.de/

Global warming causes vectors for emerging diseases to spread further and further North

Science can only react

The 'Transmission, Prevention, and Reporting of Emerging Infectious Diseases' programme for the International Conference IMED 2016 in Vienna, this November, reflected events in the field of emerging diseases that have occurred over the last two years. Therefore, key congress topics included the Zika virus, the effects of global warming and the unusually high number of hospital-acquired infections (HAIs) caused by MERS-CoV. 'With all emerging diseases, science can only ever react to them,' emphasised Austrian virologist Professor Norbert Nowotny, a local scientific organiser and member of the scientific committee at IMED, who spoke with European Hospital at the event.

Infections caused by the Zika virus present a very broad clinical picture. In 2015, when problems in the unborn babies of infected pregnant women were first observed, the cardinal symptom was microcephaly. However, it has since been discovered that the typical cerebral anomalies (reduced volume, calcifications or malformations of the cortex) can also occur in children whose heads are of normal size.

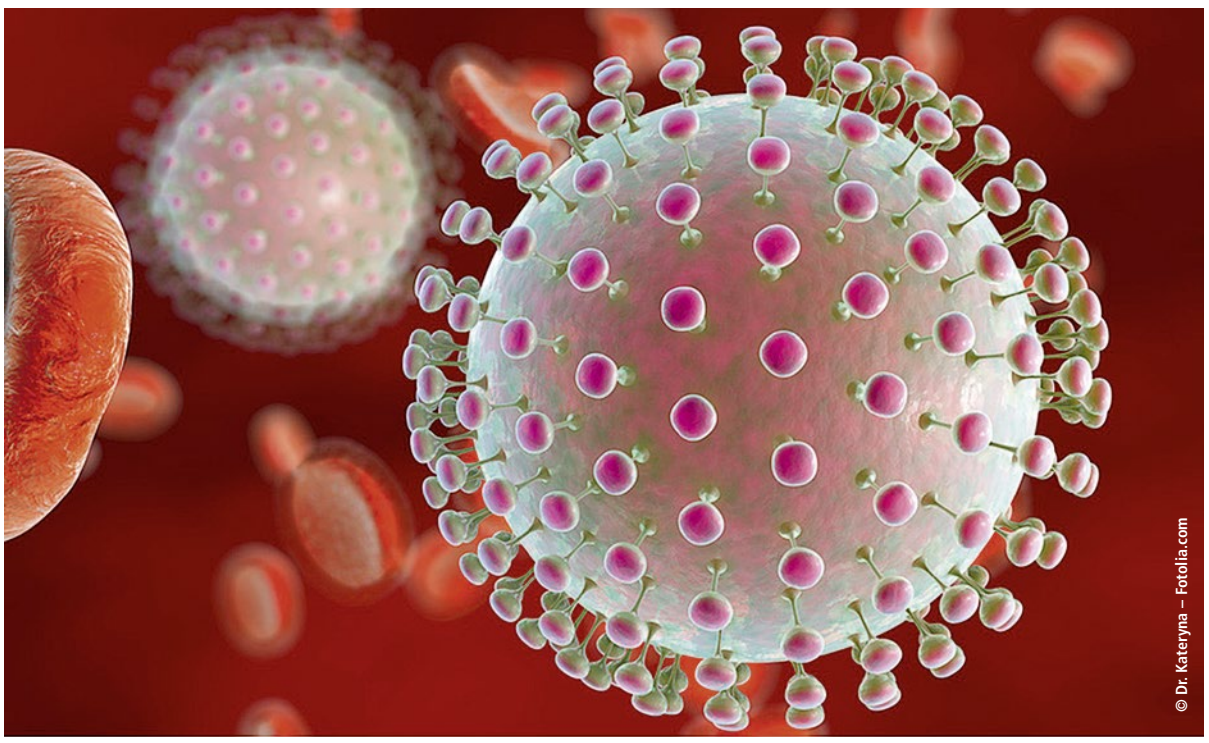
The clinical picture has also been significantly extended, with malposition of the hands and legs now also frequently diagnosed.

Furthermore, there are indications that an infection with the Zika virus can also lead to severe clinical symptoms in adults.

'The diagnosis of the Zika virus, along with all other types of Flavivirus, is still a big problem,' Nowotny points out. With Flaviviruses, the time span in which the virus itself, or its molecular footprints (e.g. via polymerase chain reaction) can be detected is relatively short, and the serological tests available (Zika Virus Immunoglobulin-G and M) cause massive cross reactions with other Flaviviruses, such as with the pathogens causing Dengue fever, Yellow fever or West Nile fever. Considerable research is still needed, Nowotny explains.

Norbert Nowotny PhD is a Professor at the Institute of Virology in the University of Veterinary Medicine, Vienna, and Professor for Virology at the Mohammed Bin Rashid University of Medicine and Health Sciences in Dubai, United Arab Emirates. The virologist researches all aspects of infectious diseases (particularly viral related) in humans plus domestic, zoo and wild animals. He also specialises in medical and veterinary medical entomology, viral infections spread by mosquitoes and ticks, emerging infectious diseases and zoonoses. His work as local scientific organiser and member of the scientific committee at the IMED 2016 is a role he has held at five previous IMED congresses.

To replicate, a virus needs to hijack mechanisms within our cells



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Global warming causes the vectors for emerging diseases to spread further and further North. Although Aedes aegypti, the transmitter of Dengue fever and Chikungunya fever, has not yet managed a breakthrough into Europe, Aedes albopictus, a type of mosquito and close relative, has now spread across the entire Mediterranean, and can also function as a transmitter for both those diseases.

Spread via infected holidaymakers bitten by this species of mosquito, there has already been a local Dengue fever outbreak in Dubrovnik, Croatia, and around 200 people developed Chikungunya fever in Ravenna, Italy. These outbreaks were only contained with the help of a massive chemical fight against the transmitters. 'This shows how important monitoring systems are,' Nowotny emphasises. This is not only important in the Mediterranean countries: 'Aedes albopictus is on the brink of crossing the Alps,' the virologist warns.

'For hospitals, MERS-CoV is a big problem,' he stresses. There has been an unusual increase in hospital infections through this viral agent, which originates in the Arabian Peninsula. Only 5% of those infected had direct contact with dromedaries, which act as vectors for this infection, and the remaining 95% of infections were transmitted from human to human – within the family, in the community and frequently also in hospitals.

The hospital acquired infections were initially limited to Saudi Arabia but, in mid-2015, at least 186 people became infected in South Korea (of whom 36 died) after an infected traveller who had returned home from a trip to the Arabian Peninsula had sought help in several hospitals. 'There is not yet sufficient research into the problem of why there are so many hospital-acquired infections from MERS-CoV,' Nowotny reports.

Although travellers have now spread the virus throughout many countries there have not yet been any cases of hospital acquired infections involving the MERS Coronavirus outside the Arabian Peninsula and .Korea.

Hospital

A leading British medical organisation has issued a hard-hitting report that paints 'a grim picture' of the National Health Service (NHS), Mark Nicholls reports

The document from the Royal College of Physicians (RCP), entitled 'Underfunded, Under-doctored, Overstretched – the NHS in 2016', highlights challenges facing the health service across the United Kingdom.

The report depicts the NHS struggling to cope under the increasing pressure of rising demand and inadequate funding, with resulting workforce pressures threatening patient safety.

Drawing on views ranging from senior consultants to trainee physicians, combined with on-going evidence of the scenario facing the NHS, the report outlines key areas of concern, yet also offers recommendations for government action.

It comes as health trusts are facing financial shortfalls with recorded hospital deficits hitting £2.45 billion and as junior doctors have contin-

Brexit: Uncertainty in every question

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of policy confusion there. One thing is clear: The UK will struggle to play any significant role in these global debates, which is a pity.'

Brand: 'I totally agree. Momentarily, we obviously live in times of so called Post-Truth-Politics, where everyone can spread untruths in politics online via social media and offline, and people do believe it. The best example is the claim about these £350 million that were transferred to the EU on a weekly basis and which was the very first thing politicians backed up on directly after Brexit.'

Helmut Brand is Jean Monnet Professor of European Public Health and head of the Department of International Health at Maastricht University, the Netherlands. The professor studied Medicine in Düsseldorf and Zürich and holds a master's degree in Community Medicine from the London School of Hygiene and Tropical Medicine and London School of Economics. He is president of the European Health Forum Gastein (EHFG) and co-chair of the European Alliance for Personalised Medicine (EAPM).

After Brexit is completely concluded, what will happen to all the physicians working abroad in common projects at universities and clinics?

McKee: 'First, who can tell whether Brexit ever will be concluded? Second, this is a very good point. Universities in the UK were unanimously opposed to Brexit, recognising that the consequences would be devastating. The same is true for the NHS, which depends on EU citizens in so many areas.

'Some British politicians talk about giving EU citizens already here the right to remain, but that simply reveals their ignorance of the issues involved. These workers have many rights, as EU citizens, including entitlement to healthcare should they retire to other member states after retirement or when they travel home while employed in the UK, as well as portability of pensions etc. I see no evidence that these issues are being addressed.'

Brand: 'The most important thing is that there exists a date for the exit. Now, the European Commission has to deal with the question of where the European Institutions will move and what to do next. Several good people are already leaving, returning to their home countries.

'I personally know neurologists who are concerned about the fact that they might have to leave Horizon 2020, which is not a question of financials in first place, but a question of the existing and established networks. Big projects cannot be stemmed solely. If Britain leaves such projects because of Brexit an important partner will be lost. This is definitely something both sides will suffer from.'

What's next?

McKee: 'It really is impossible to predict. The Scottish First Minister was asked, after she met Theresa May, whether she was undermining the government's plans. She pointed out that there was nothing to undermine.

'I can only conclude that the British government is lost, with no idea where it is, or where it wants to go. There are many options, from no Brexit, through soft Brexit, and hard Brexit. All are, for one reason or another, "impossible". The challenge is to find the least impossible solution, which may just be remaining a member of the EU.'

Brand: 'I think that an important question for the Healthcare Sector will be how to deal with standards. We do have standards for drug approvals, in medical technology, regulations for treatment and therapies, there exists a joined procurement for ordering vaccines, and all these are European standards.

'The question is, what will Britain do? Will it stay with these established standards or, for example, draw near the USA. The second could lead to a lot of problems. These are questions that have to be faced.'

Professor Martin McKee qualified in medicine in Belfast, Northern Ireland, with subsequent training in internal medicine and public health. As Professor of European Public Health at the London School of Hygiene and Tropical Medicine he was founding director of the European Centre on Health of Societies in Transition. He is author of over 900 scientific papers and 44 books and is Fellow of the Royal Colleges of Physicians of London, Edinburgh, and Ireland and the UK Faculty of Public Health and a former chair of the UK Society for Social Medicine.

The NHS needs urgent treatment

deficits hit £2.45 billion

ued to stage strike action.

The RCP report focuses on three key areas, outlining the organisation's findings in each:

Underfunded: The report says the NHS budget has not kept pace with rising demand for services, suggesting demand increases by 4% every year but, in real terms, NHS funding will increase by only 0.2% per year to 2020, whilst social care cuts are piling pressure on NHS services.

Under-doctored: The RCP suggests the UK does not train enough doctors and with the number of medical students having fallen, there is a shortage of doctors training to be medical specialists and unfilled consultant and nursing posts in many hospitals.

Overstretched: Four in five physicians-in-training report that their job causes them excessive stress and 95% suggest poor staff morale is having a negative impact on patient safety in their hospital.

RCP registrar Dr Andrew Goddard said: 'It is clear to all of us working in the NHS that we are at a point of no-return and the NHS in its current form is unsustainable without a significant increase in funding. We can't continue to provide ever-more expensive treatments to an ever-increasing group of patients and not expect the system to collapse.

'As doctors, we see the problems this creates on a daily basis, be it at the front door of the hospital, in A&E, or in out-patients. Patients can see it too and realise that the NHS is no longer the envy of the world and isn't fit for our changing world.

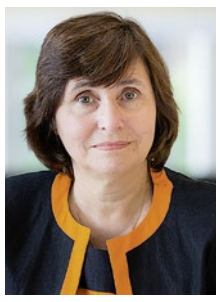
'There are some big decisions that society has to make and the political parties have to stop blaming each other for where we are and work together to build a health and social care system that is fit for the UK in the 21st century.'

The RCP report points out that the pressures of an under-funded, under-doctored, and overstretched NHS put patient safety and recovery at risk with patients are facing longer waits for treatment and delays in discharge. More hospitals are temporarily closing their doors owing to pressure on beds and staff, throughout the year rather than just in response to winter pressures.

The RCP is calling for a better-funded NHS that meets the demands of patients, with a budget that meets the demand for health services; sets realistic targets for efficiency savings; protects funds for transformation; and invests in the long-term sustainability of the NHS.

The organisation wants more doctors to be trained to provide enough doctors across all parts of the medical workforce, from GPs to physicians as well as specialists; incentivise doctors to work in the most challenging and in-demand areas of medicine; and address nurse shortages and promote innovative models of staffing, such as physician associates working alongside doctors.

The RCP also wants to see improvements in the working lives of NHS staff. RCP President Professor Jane Dacre said: 'As a doctor, I realise this is a tough diagnosis for the NHS. However, a diagnosis is the first step towards working with colleagues to find solutions. We are keen to find the best treatment for the NHS over the coming weeks, months and years.'


Jane Dacre, RCP President


Andrew Goddard MD

At the heart of Catalan Health Minister's strategy

Big Data, de-privatisation and independence

Catalonia, Spain's richest region, is launching one of the largest Big Data healthcare projects in Europe, after scrapping a polemic plan that would have enabled patient data to be shared with private for-profit companies. As the region confirms its leading role in healthcare technology, it is also de-privatising key hospitals to improve efficiency in a context of low funding, a decision that has received considerable attention in Spain. Antoni Comín i Oliveres, the Catalan Health Minister, came back on these highly discussed issues and explained what other challenges lie ahead for his region in our exclusive interview.

Report: Mélisande Rouger

The Visc+ project was intended to collect all patient data in Catalonia. The Health Minister's administration dropped this last summer. What will happen now?

Comín i Oliveres: 'It's important to remember that Big Data generates a lot of concern, especially regarding data confidentiality and information security. There are also concerns as to who will benefit from that information, i.e. public entities to improve healthcare or private companies for their own interests. Many questions remain open.

'Big Data is fundamental to pursue health investigation, so it's crucial for any project to be consensual both at the political and social level. We couldn't have such a controversial programme as Visc+. We couldn't have any plan that caused suspicion and defiance in politicians and among the public.

'We held participative meetings with scientists, experts, researchers and social and political representatives, to let everyone explain their views on Big Data. All parties also signed a common resolution in Parliament

'Our new plan is called PADRIS (programme for health research and innovation analysis) and will be implemented by the end of 2016. It will enable massive data analysis for research purposes using our seven million patients database and the database of the Health Catalan Institute. This is the second biggest Big Data plan in Europe after the United Kingdom.

'Only research centres accredited by government will be able to use that information. These include non-profit private research groups such as the Puigvert foundation or the Sant Joan de Déu Hospital.

'This will guarantee no one can make business with the citizens' clinical history.'

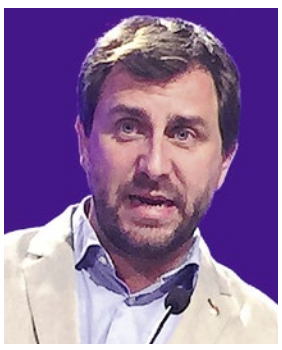
A lot of controversy also surrounds your decision to buy back the activity of Clínica del Vallès in Sabadell from the Quirónsalud group…

'This is creating a lot of political debate, but really it is quite simple. We are following the provision model defined in the Catalan Health Law in 1990, according to which the government must employ public hospitals first, and only if necessary privately run institutions – and then the government should work with non-profit private groups first. We are following this principle of preference.

'The hospital activity purchase system had become messy over the years and we tied it up. Providers are very influential, but our mission is to guarantee maximum quality, equity and efficiency.

'The activity at Clínica del Vallès could be done by two public hospitals: the Parc Taulí, also located in Sabadell, and the Consorci Sanitari, in nearby Terrassa. We have relocated two thirds of the activity in Taulí and a third in Terassa. We also save €1 million in the process.

'You don't need to be left wing to do this. Adam Smith said that private companies needed to compete in the market and criticised monopolies. However, a hospital consortium is like a small monopoly, limited in time and space. How can a company be competitive inside a monopoly?'



Antoni Comín i Oliveres (Toni Comín) is the Catalan Health Minister under Carles Puigdemont's administration, composed of Junts pal Si ('Together for Yes'), the pro independence coalition formed by Convergència (right wing) and Esquerra Republicana (left wing) in 2015. Comín, a professor of social sciences and a philosopher, became a socialist deputy in June 2004. Proposed by Esquerra Republicana, he was appointed Health Minister.

Are you then planning to buy other hospitals from private companies?

'We are in talks with Quirónsalud concerning the purchase of the Hospital General de Cataluña (HGC), located in Sant Cugat. In 2005, the administration had planned to build two hospitals in Rubi and Cerdanyola, which are very close to Sant Cugat.

'Experts have estimated the purchase would cost us €55 million. It's actually cheaper to buy the HGC than to build two new hospitals. That's a lengthy and costly process and, right now, there's no money for that.

'In addition, we could transfer basic healthcare activity to nearby hospitals in Terrassa and Taulí, and let the HGC do all the specialised work. Right now it's the other way around and basic care hospitals provide specialised care, while the HGC provides basic care. It's the world upside down.'

How will you tackle waiting lists, one of Catalonia's major problems?

'Last June, there were 161,730 people waiting for surgery, 3.1% more than a year ago. There were also 4.7% less patients waiting for diagnostic examinations. About 100% cancer patients had received surgery in less than 45 days and almost every heart surgery patient had waited less than 90 days.

'Our plan is to reduce the waiting list for surgery and diagnosis by 50%, by improving information access, empowering primary care, increasing the proactivity of our healthcare system and augmenting activity. We need €100 million to do it. 'To reduce the list to nought, we would need €1,000 million!'

How does Catalan healthcare compare to the rest of Europe?

'I'd like to have an OCDE PISA report for Catalonia; I think we'd rank very high. We have a very good, high quality model, which is very linked with research and uses a large diversity of providers.

'However, we have three major problems: waiting lists, wages and the fact that our foundations haven't received a cent in years because of the crisis. Some hospitals are also ageing pretty fast. All of these issues are solvable with money and that is why we want to cancel our annual €16,000 million deficit – the biggest in the EU. We're the only region in the EU with an 8% budget deficit. For us, the only way to do so is to become independent.'

From desktop display to large formats, projection and LED modules

Opt for state-of-the-art visual technology

In today's digitised world, hospitals are already embracing the benefits which technology brings to improve efficiency and reduce costs. Against a backdrop of stretched resources and operational scrutiny hospital managers are able to address the needs of multiple stakeholders through hospital-wide digitisation. Improving communication using digital signage for way finding, check-in, queue management and info/entertainment helps to enhance the patient and visitor experience and alleviate potential frustration. In clinical practice, collaboration is essential to maximise productivity and synergy of talent requiring visual access to patient information to ensure best patient outcomes.

To assist in the challenges of hospital-wide digitalisation, NEC is the only manufacturer able to offer such a wide portfolio of display products, including desktop and large format displays and projection, as well as fine pitch LED modules. This unique position means that NEC can recommend the best fit solution to virtually any application scenario with a customer oriented consultative approach. Trusted NEC quality is the benchmark for performance and longevity with a long heritage serving the special needs of the healthcare sector.

Ready access to up-to-the minute information will help to improve the patient and visitor experience. Touch screens allow visitors to check-in and receive directions for their onward journey through the hospital building. Video walls and large format displays provide way finding information and can be instantly updated to provide emergency messaging, should the need arise.

Delivering excellence in patient care demands effective multi-discipline collaboration. The Multi-Disciplinary Team (MDT) facility is critical in assembling healthcare practitioners to collaborate with full access to patient data and multiple PACS images, side by side, viewable by large numbers of people, both in one room and via remote conferencing. NEC's large screen UHD displays deliver images equivalent to 8MP presenting unprecedented richness of detail and pixel-free viewing on a huge scale with controlled colour reproduction and consistent images viewable from all angles. Projection solutions, also available in 4K resolution provide additional options for break out rooms and training centres.

Digitised information signage systems – a visible profit for everybody

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In a caring profession, there is no substitute for the personal touch, but with NEC as your partner, hospitals can benefit from state of the art visual technology to improve patient confidence and deliver an exceptional healthcare service.

* Source: NEC Display Solutions

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The global migration mapping project

Combatting internationally infectious diseases

Report: Mark Nicholls

Experts at a university in the United Kingdom have designed a large-scale data and mapping project that they hope will help in the global fight against infectious diseases.

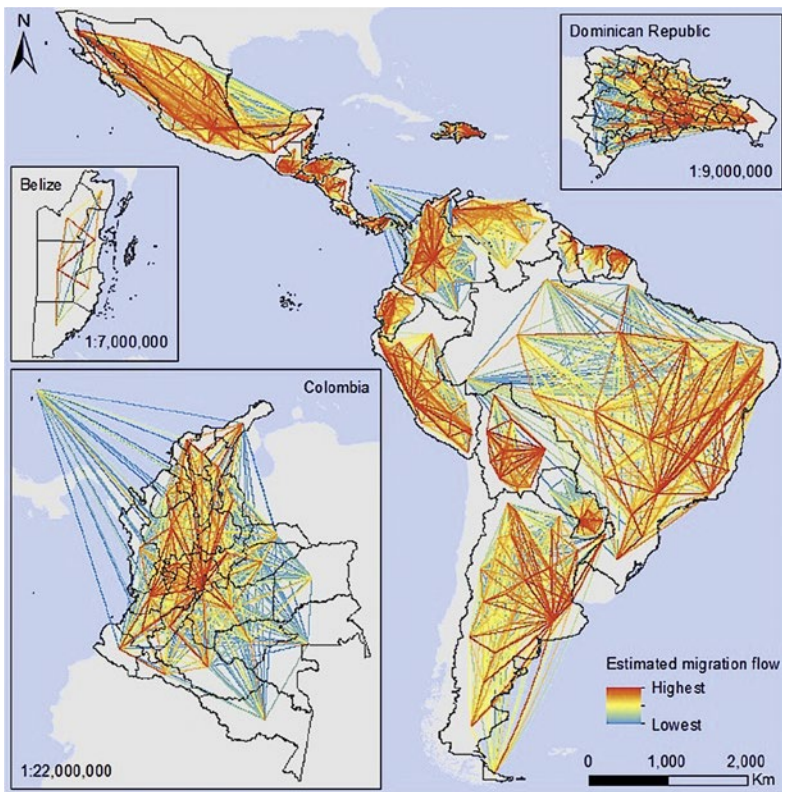
The model, completed by geographers at the University of Southampton as part of the WorldPop project, tracks the flow of internal human migration in low and middle-income countries.

This has, for the first time, mapped estimated internal migration in countries across three continents; Africa, Asia and Latin America and the Caribbean.

A key focus of the work at this stage is on malaria, where an understanding of how people move around within countries is a critical factor in combatting a disease in which the parasite that causes it can easily be reintroduced into malaria-free areas by mobile populations.

In collaboration with the Flowminder Foundation, and supported by the Bill and Melinda Gates Foundation, the researchers used publicly-available census micro-data to model estimates of migration flows within countries and then produced a series of maps to visually represent the data.

They examined anonymised details of individuals' residence, number of years spent there and previous residence. 'We sourced the census data from around 40 different countries and have produced detailed population migration maps on a scale not seen before,' explained lead author Dr Alessandro Sorichetta, from the university's Geography and Environment department. 'They show webs of connectivity within countries – indicating high and low flows of people moving between different locations.'



Estimated internal human migration flows between subnational administrative units for every malaria endemic country in Africa. Source: WorldPop

The aim is to support malaria control and elimination, strategic planning in endemic countries through identifying relative strengths of connectivity among different areas, and use them to understand malaria transmission dynamics in endemic countries, he added.

Against this backdrop, figures from the International Organisation for Migration and The World Bank show that, without accounting for seasonal and temporary migrants, more than one billion people live outside their place of origin.

Meanwhile, human mobility is expected to continue to rise, creating a range of impacts, such as invasive species, drug resistance spread and disease pandemics.

'It's crucial we understand human mobility, so that we can quantify the effect it has on our societies and the environment, and provide strong evidence to support the development of policies to address issues, such as public health problems,' he underlined.

The researchers are now integrating the migration estimates with data on malaria prevalence – helping to inform regional elimination and global eradication plans for the disease. 'In this context, we'll go within subnational communities of malaria movements and identify sources of transmission,' he continued. 'The idea is to combine malaria prevalence data with the estimated migration flows to derive estimates of how well different areas are connected in terms of relative amounts of parasite movement.

'The main benefit is using the model to track the spread of infectious disease but also to understand the drivers affecting the distribution of these diseases.'

Researchers also believe the data could be used to support regional control and elimination strategies for other infectious diseases such as schistosomiasis, river blindness, HIV, dengue and yellow fever. 'The project could lead to being able to better control and tackle these diseases by focusing resources and allocating them to areas where they are most needed, to inform eradication and elimination planning and tackling these disease in a more cost-effective way,' Sorichetta pointed out.

There will also be benefits in helping inform decisions in trade, demography, transportation and economics, he said. However, the study team does acknowledge limitations to the data set because seasonal migration is not captured by the censuses, nor movement triggered by war and natural disaster.

Professor Andy Tatem, Director of WorldPop, said: 'Understanding how people are moving around within countries is vital in combating infectious diseases such as malaria. The parasite that causes the disease can be quickly re-introduced to a malaria-free area by highly mobile populations. Having an accurate overview of how different regions of countries are connected by human movement aids effective disease control planning and helps target resources, such as having treated bed nets, or community health workers, in the right places.

'Having data for all low and middle income countries across three continents will greatly aid disease control and elimination planning on global and regional scales.'

The WorldPop project was initiated in October 2013 and aims to provide an open access archive of detailed spatial demographic datasets for Central and South America, Africa, and Asia to support development and health applications.

Dr Alessandro Sorichetta is a Geography and Environment Research Fellow at the University of Southampton, where he is mainly involved in the projects 'WorldPop' 'Human Mobility Mapping', and 'Mega Urban Changes and Impacts in the Decade of 2000s'. His interests include GIS and Remote Sensing, spatial demography and epidemiology, human migration and urbanisation and its effect on environmental matrices.

Professor Andrew J Tatem directs the WorldPop Project and co-directs the Flowminder Foundation. He focuses on the application of spatial demographics in malaria burden estimation, maternal and newborn health, dispersal of diseases and their vectors through global transport networks, and quantifying population movements in relation to disease dynamics.

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Diversity is the enemy

x-Health: Demands for real interoperability

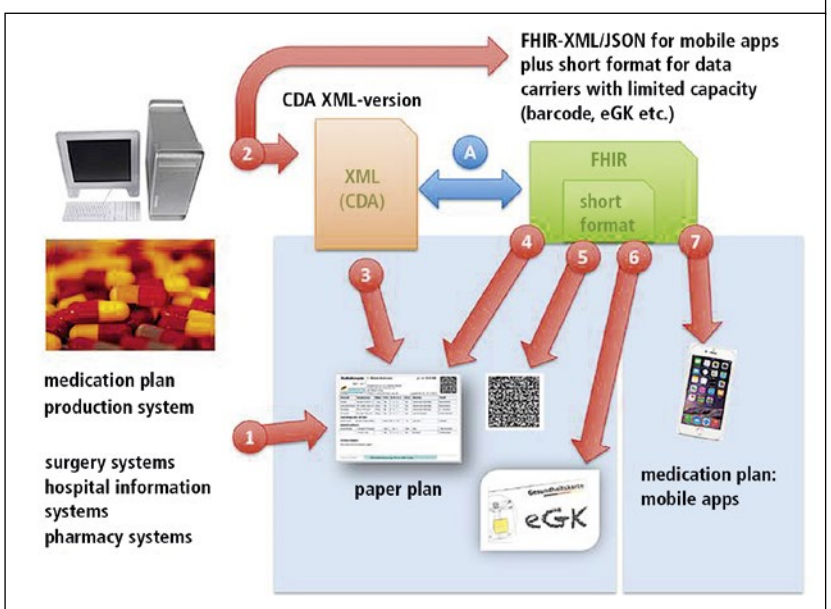
Britta Böckmann, Professor for Health Informatics at the Technical University of Dortmund summarises the lack of feeling for terms such as eHealth, mHealth and telehealth with the description xHealth. However, xHealth also stands for Exchange, 'that is interoperable solutions, meaning actual interoperability and data exchange not seen in previous approaches,' Böckmann explains. She views the current direction with scepticism and calls for a consensus-based eHealth strategy for Germany.

A workshop held before this year's conhIT and attended by representatives from the German Parliament, medical insurers and health informatics firms, tried to open up an international perspective and to answer the question if Germany's current position regarding xHealth. Participants compared patients' access to digital services within the health service and access to their own data.

The question: Are patients participants in the digitisation or is it only affecting service providers? The country-specific eHealth strategy was also scrutinised. 'Unfortunately the result shows that Germany is in last position compared to other countries,' Böckmann says.

To a large extent this is due to the number of different players working on the subject of digitisation. However, she does not believe it would be possible to implement a centralised system in Germany such as the one introduced in Denmark. 'Our health system, with its federal structure, cannot support this. Self-administration, with different associations representing the service providers and funding bodies, makes this centralisation impossible.'

Whilst Austria is automatically introducing the electronic patient file (ePA) for everyone via the e-card, the plan in Germany is that citizens must act. 'People themselves will have to apply for the use of services such as the ePA per electronic health pass. However, this plan has an inherent danger of a silent, large majority developing who will do nothing and therefore will not have access to these modern, digital services, in the same way as this was discussed around the topic of organ donation. Therefore, the switch from analogue to digital for routine processes in doctors' surgeries, for example, will only happen very slowly. From a systems and health informatics point of view a centrally controlled approach taking international standards into account and making digitisation part of routine care would obviously be wonderful,' Böckmann believes.



Overview of the formats used: Systems with a medication plan for patients can, for instance, directly print a paper version for the patient (1). The plan is stored electronically in CDA format or FHIR format/ultra short format (2). CDA and FHIR/ultra short format can simply be transformed into one another, both ways, with generally available tools (bijectivity, A). Paper versions can be produced from CDA (3) as well as FHIR/ultra short format (4). The short format is also suitable for the barcode (5) or the eGK (6). The FHIR base format is available for mobile apps (7).

More focus on the patient

The introduction of an electronic health card would shift the interests of the patient to the fore. The eHealth law states that Gematik (the company in charge of the electronic health card development) will have to develop certain specifications, such as the electronic patient record, by 2018. 'Unfortunately, the actual plans are oblivious to current technologies and possibilities because they hold on to principles developed at a time when there were neither smartphones nor apps,' the professor points out.

One example of this is the medication plan. Conceived initially on paper, in the second step it is to be introduced in electronic form and stored on the patient card. 'However, the patient will have to carry it around as a paper version because they will not be able to access their own data stored on the card beyond the surgery, i.e. without a health professional card (HPC), due to the legally prescribed two-key principle. In my view, this is completely the wrong approach and will reduce public acceptance of this card even further,' Böckmann states. 'An increasing number of health insurers now offer their patients apps. There are also numerous telemedicine projects, and the technology is developing at a rapid pace, but the way things are now this could lead to a two-class society. Whether a diabetic patient will have an app financed will depend on their insurer. Whether or not heart failure is treated telemedically, of whether a patient is even told about this option, depends on whether the combination of the doctor in charge of treatment, the location of the patient and who they are insured with, happens to be covered by one of the pilot projects. But surely it shouldn't be like that,' she says, displaying anger.

A clear mandate for the future

There was a clear call for a consistent eHealth strategy for Germany that was also discussed during the workshop: 'The law on eHealth only covers certain aspects and mainly introduces the infrastructure. It consists of a collection of regulations which, although meaningful in parts, does not follow any overall strategy,' Böckmann complains. 'The interoperability register is only a collection and evaluation of existing projects which utilise certain standards instead of clear rules as to which standard is to be used in which cases and settings, which would be the only way for manufacturers and users to adhere to them. Diversity is the enemy of interoperability here.'

There is also the financing issue. Böckmann: 'xHealth services, being inter-sectoral building blocks, often fall into the gap between out- and in-patient treatment, as telemedical care concepts often have in-patient as well as out-patient aspects. We've been practising telemedicine for 20 years, but there are only two reimbursable items in the billing catalogue. On the other hand, the postage for a doctor's letter is very easy to reimburse.'

However, Böckmann does point to evidence of progress in the medical fraternity. 'The State Medical Association in Baden-Wurttemberg is now accepting applications for, and evaluations of, telemedical projects involving remote treatment. This means that the ban on remote treatment is finally put under scrutiny, and it is the first time that things are moving on the part of the medical associations, with other federal German states watching this development with a lot of curiosity.'

Britta Böckmann has been Professor for Health Informatics at the Technical University of Dortmund since 2006. Her focus is on telemedicine and telematics, digital care management for integrated care, trans-sectoral treatment and information systems in healthcare. Böckmann also heads the scientific advisory board at DGTelemed, the German Association for Medical Informatics, Biometry and Epidemiology (GMDS) telemedicine working group and the working group on health informatics at the Institute for Medical Informatics, Epidemiology and Biometrics at the University of Duisburg-Essen.

Expertise of JVCKenwood and Totoku joined for another display product

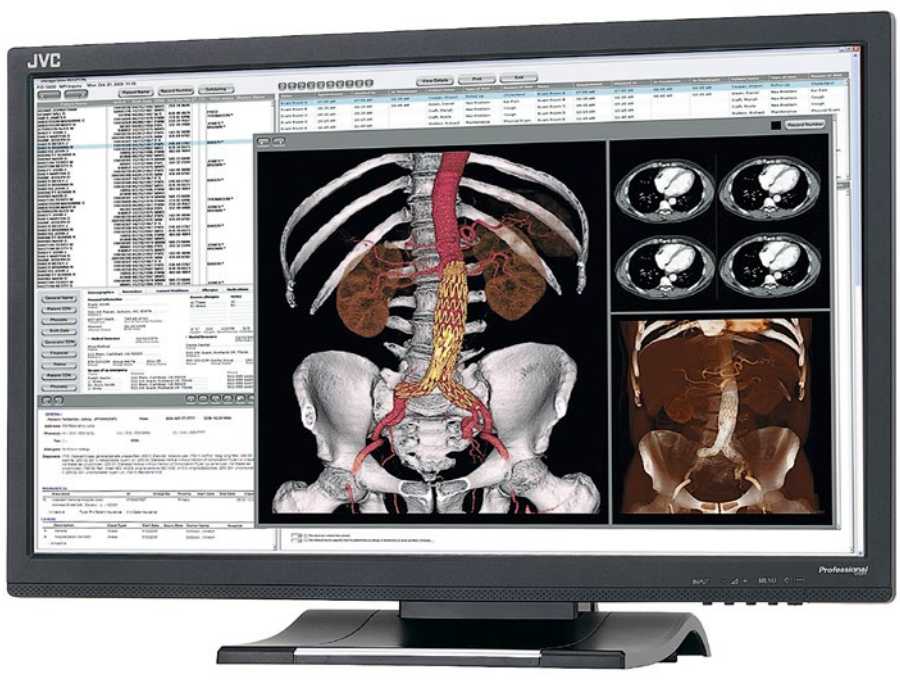
Introducing the DICOM preset monitor

Since JVCKenwood Corp acquired the display manufacturer Totoku three years ago the expected synergies in the development and distribution of common solutions and products have been set, according to Marcel Herrmann, Marketing Manager for Medical Displays at Totoku: 'We wanted to combine our expertise and gradually develop new areas and applications – and we've succeeded.'

Their first product was a display for endoscopy. 'Our mother brought her expertise from the broadcasting sector, and we have the knowledge for specific requirements in healthcare facilities,' he pointed out. During the European Congress of Radiology in March this year, the company first launched its video solution based on a 4K video-capable camera from the broadcasting field.

The next screen, jointly developed by JVCKenwood and Totuku, is the GD-W213L. This high-resolution 16:9 widescreen LCD / LED monitor with a size of 21.5 inches is reported to be particularly suitable for reviewing. 'It has a high contrast ratio of 1,000:1 with 1920 x 1080 pixels and, thanks to an anti-reflective screen, a wide viewing angle. For high quality, bright and sharp images, the LED backlight has a brightness of 250cd / m²,' Herrmann explains.

Besides this, the GD-W213L offers an integrated power supply, audio inputs for HDMI, DVI and RGB and a multilingual menu that allows operation in German, English, French, Spanish and Japanese, the manufacturer reports. 'The aspect ratio is adjusted automatically. A DICOM preset ensures realistic reproduction of all xray images.'



Hospitals need a holistic approach to cyber security

Hospitals and healthcare providers are being urged to adopt a holistic view of cyber security to help protect critical patient data, Mark Nicholls reports.

A number of organisations within healthcare remain at risk of leaving systems vulnerable by failing to ensure there is a broad range of protection in place to safeguard data from hackers or cyber attack.

IT expert Dr John Lockley, Clinical Lead for Informatics with the Bedfordshire Clinical Commissioning Group (CCG) in the UK, also believes healthcare providers need to factor in more elements alongside IT considerations.

In a presentation at the EHI Live event in Birmingham, entitled 'A holistic view of healthcare cyber security', he suggested it was wrong to think of IT in isolation:

'We have to consider what IT interacts with – programmes interacting with patients, the paperwork, protocols, processes and pounds, as well,' Lockley explained. 'We need also to remember that people are involved and how they and their psychology work.'

This is not just about individuals falling for phishing emails and clicking on unauthorised websites, or hospitals installing advanced virus blockers and other firewall safeguards, but also in ensuring staff are adequately trained in how to respond to such threats.

Additionally, personnel need the time, a robust infrastructure, and the correct hardware and software needed to carry out their roles correctly and safely.

Dr Lockley said that the National Health Service (NHS) often invests heavily in certain parts of the system but fails to guard against 'back door' attacks on the more vulnerable aspects of their IT.

He also warned that systems running unsupported software, such as Windows XP, were particularly vulnerable to attack and added: 'My advice is for hospitals to spread resources carefully and thoughtfully in terms of cyber security and educate and train staff.

This means having money available to buy in people to do the teaching and then giving staff the time to receive the training.'

Equally, hospitals should not go to the opposite extreme of having so many technical and procedural checks inserted into their systems that it can actually prevent people from working efficiently.

With NHS organisations now working more closely with local authorities, as health and social care come together, the health service need to ensure it is not left vulnerable when linking with outside bodies that have older, or more vulnerable, IT systems and equipment.

Health remains a prime target for hackers and the consequences of not adequately protecting data can be devastating, with patient and clinical information potentially lost, encrypted or even altered by hackers.

'The first priority is, take regular backups; the second priority is to ensure that you've put in all the latest software patches; and the third element is to train the staff to think carefully about what they are doing and not automatically click on links of open documents just because they are there,' Dr Lockley advised. 'Cyber security also needs board level priority and it's important to have the IT team available 24 hours a day to respond.'

Hospitals and healthcare providers also should be aware that it is not always straightforward to upgrade to the latest versions of software, because that may impact, or not be directly compatible, with other parts of the system.

'Overall,' Lockley added, 'when it comes to cyber security, hospitals should think holistically and not just about the software, or the hardware, but also remember to give ordinary front-line staff enough training in cybercrime awareness - and then give them enough time to put these defensive procedures into action.'

Dr John Lockley is the Clinical Lead for Informatics for Bedfordshire CCG (Clinical Commissioning Group), chair of SystmOne National User Group and a member of the eReferral Service Programme Board and Electronic Referral Advisory Board. He is also Deputy Chair of the Board of Bedfordshire and Hertfordshire LMCs Ltd and Chair of Beds and Herts LMC IM&T advisory group

From high-end to demanding hybrid cardiovascular surgery

Plug-in and go with a hybrid

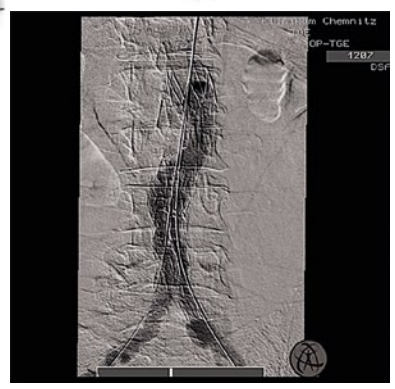
As the aged population is increasing, the need for demanding interventional cardiovascular procedures as well as high-end orthopaedic, trauma and spine surgery increases and will continue to rise. For those complex, time-consuming and X-ray-intensive procedures with high imaging requirements, hybrid operations are more and more a standard procedure. The hybrid OR offers enormous advantages for this type of surgery: it reduces risks and stress for the patient and minimises surgical time.

The company Ziehm Imaging reports: 'With the Ziehm Vision RFD Hybrid Edition you can extend your clinical capabilities from high-end surgery procedures to demanding hybrid cardiovascular surgery, everywhere, anytime. With its zero room preparation, the comprehensive mobile hybrid solution allows you to plug in your system and start your procedure.

'The Ziehm Vision RFD Hybrid Edition is the first fully motorised mobile C-arm. The powerful 25 kW generator and Advanced Active Cooling enable excellent image quality.'

Installation and operating costs, adds Ziehm, makes this model an 'ideal system to perform strongly in complex surgical and interventional procedures. For surgeons, the mobile hybrid solution is a smart choice in comparison to fix installed systems as it does not require any additional room preparation.'

According to Sven Seifert MD, Head of the Department of Thoracic, Vascular and Endovascular Surgery, at Chemnitz Hospital, Germany: 'The future belongs to the mobile hybrid OR. The mobile C-arm with the image quality that we have experienced offers a space-saving and cost-efficient alternative to a fixed unit.'



Control image with CO_2 contrast media, endovascular aortic repair (EVAR). Courtesy of Chemnitz Hospital (right)

Success for a complete diagnostic radiology solution

Going fully digital in a single key stroke

Installing a complete diagnostic radiology solution to network six sites of a hospital group, to process, manage and archive image data acquired across all modalities, is a 'challenge', acknowledged by Professor Dr Peter Landwehr, Medical Director of the Clinic for Diagnostic and Interventional Radiology of Dikovere Henriettenstift, Hanover, Germany. In 2010, he and his team overcame that challenge and they are extremely happy with the results. 'Why didn't we do this sooner?' asked those involved in sourcing and implementing the solution.

CT and MRI imaging have brought increasing expectation of faster access to image data

How it all began

A complex tender procedure to purchase diagnostic radiology viewer, enterprise archive and an enterprise viewer solution resulted in six manufacturers being short-listed. For the final decision, comprehensive requirements documents and detailed specifications were drafted and systematically evaluated by a fifteen-strong committee representing all user groups and the IT department.

Understanding how the technology is supported in a real-life clinical setting is just as important as the technology itself. An experienced consultant familiar with the market supported the committee. 'It was crucial for us to have professional expertise on board because this was our very first diagnostic radiology solution.' The Hanover-based hospital group was a 'digital radiology late-adopter' due to a drawn-out process when the legal structure of the local hospitals was turned into a holding. 'Since we were lagging behind, we wanted full adoption from day one,' Landwehr recalls. A precise needs assessment and an operational plan were established aiming to optimise the cost-benefit ratio while avoiding common deployment mistakes.

The winner is...

Finally, the selection committee unanimously opted for the provider they considered offered superior functionality and support: Carestream. The firm's solution scored with ease-of-use inside and outside of radiology, a slew of innovative functions, a convincing value-for-money ratio and an innovative team focused on future developments.

From analogue to digital

'Before we could put the new solution into operation we had to get rid of a few analogue standalone solutions,' Landwehr points out, adding that several CR systems had to be purchased and some ultrasound systems had to be made DICOM-compatible.

'At the same time we worked well with Carestream's DRX1,' he says. Above all the radiographers liked the wireless cassette-based X-ray solution because it offers mobility and good image quality.

Solution roll-out

Issue of the purchase order kicked off an intensive six-months' planning and implementation phase, culminating in the hardware installation: core IT components, local workstations with modern screens and reconfiguring certain modalities. At the same time several workflows were redesigned.

After ten months everything was set up. In June 2010 the countdown arrived: overnight X-ray was switched from analogue to digital. No exception allowed? Only one: a complete solution breakdown, for example, caused by network or server failure, was considered the only situation when films can be printed out. This tough stance paid off. After only a year film usage had decreased to one percent. 'For a digitisation project this is an extraordinary result, since it takes us to profitability sooner than we had anticipated,' Landwehr points out.

Positive feedback all around

Despite the staff's positive attitude towards the new digital solution, there were traces of scepticism. This is normal when a new technology is introduced that disrupts and forces changes upon well-oiled processes. "But when it ran without a hitch and everybody was comfortable with operating it the entire team was happy and we received positive feedback, not only here in radiology, but also from the non-radiology clinics we work with,' Landwehr concludes.

A system scales with the users

Six years have now passed. Quantity and quality of the requirements have been increasing constantly mainly due to images in CT and MRI, with rising expectations with regard to fast access to the image data.

The internal technology landscapes, as well as the provider's system, have continuously developed high-performance processors and huge data storage space at hospitals, new releases with new functionality at the provider's. 'We are not interested in the dernier cri when it comes to our diagnostic platform – what we do expect are intelligent and feasible solutions to optimize our workflow day in day out,' the radiologist emphasises. 'So far, the provider has met the expectations with flying colours – a fact that confirms the committee's initial decision. However, in these rapidly changing times none can rest on the laurels.

Current highlights

So far, the provider has provided fully-integrated 3D-/MPR-/MIP functionality. 'Other manufacturers can't offer comparable quality,' Landwehr believes.

He underlines the excellent workflow support, e.g. in mammography, contrast-enhanced ultrasound, functional imaging in colour duplex ultrasound and hybrid imaging.

Today the system also offers support by semi-automated assessment of oncological studies. For lesion management and size comparison current and historic images can be viewed side-by-side in MIP or 3-D and images acquired in different planes can be automatically correlated in anatomy. 'That even works across modalities with CT and MRI,' says Landwehr.

Outlook

In radiology there will be ever more data to be evaluated; ever more high-performing tools are needed to support radiologists due to scarcity in the profession. Landwehr believes radiologists with professional expertise in diagnostics and intervention will still be here in 30 years' time 'but they'll need more technological backup to meet clinical requirements'.

A system cannot simply store images and ensure access. The major task will be to provide advanced post-processing workflow such as semi-automated protocols to screen lesions, cross-referencing different clinical and imaging data sources, such as from endoscopy and pathology for clinical decision support, or an intelligent worklist assignment to optimise sub-specialty reading, thus freeing time and capacity for a radiologist to deal with complex clinical imaging questions.

'Equipped with such tools for structured reading, we will be able to meet the challenges of tomorrow and the day after,' Landwehr predicts.

Responsible radiology

While the technological support and innovative approaches by the manufacturers are indispensable, Landwehr urges radiology, as a discipline, to spearhead the development of enterprise imaging systems. Why? Dealing with huge volumes of imaging data has to be organised first and foremost with an appropriate clinical context, then to make available for clinical and scientific purposes. 'This is not something we can leave to the IT experts and industry. 'As clinically focused radiologists, we're in the best position to decide where more data will indeed translate into added value for the patient and where it won't.' A gung-ho 'Big Data will solve all problems' approach is wrong, warns Landwehr, because it will lead to 'Apple, Google and other usual suspects knocking on our doors and defining health and disease based on what's good for them. Collecting data just for the purpose of collecting does not make sense.'

Far rather, Landwehr is convinced, radiology, both in diagnostics and intervention, must be even more innovative, more clinically effective. 'Technological tools, such as a modern enterprise imaging solution, help us to become just that.'

The analogue world contained large folders of X-ray and other scans and notes all needing transportation

Professor **Peter Landwehr**, who grew up in Remscheid, birthplace of Wilhelm Conrad Röntgen, worked for 14 years in the radiology departments of universities in Bonn, Würzburg and Cologne. His seven years spent as senior physician at the Institute and Polyclinic for Radiological Diagnostics at the University Hospital, Cologne, including three and a half years as managing senior physician, increased his leadership skills. In January 2001 he was appointed medical director of the Clinic for Diagnostic and Interventional Radiology at Diakovere Henriettenstift hospital, Hanover. In October 2015 he gained a professorship from Hanover University's Medical School and, in 2016, became President of the 97th German Radiology Congress in Leipzig. In 2017 Landwehr will serve as a member of the advisory board of Röntgen's birthplace foundation in Remscheid-Lennep

Audio-visual teleconferencing with advanced remote robotics

Long distance ultrasound is not so distant

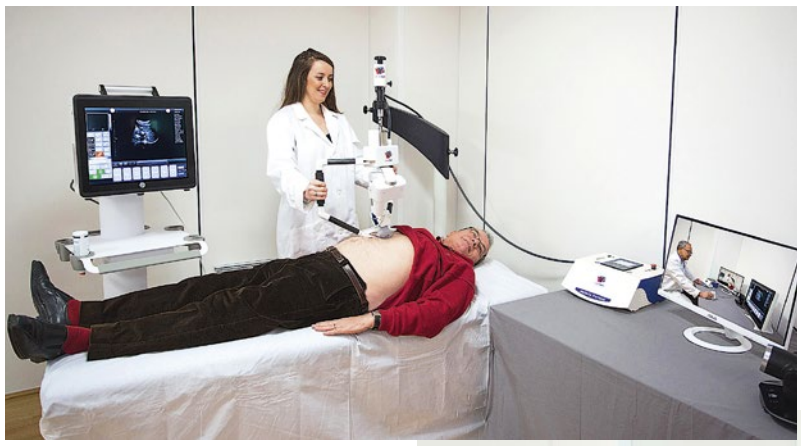
The future of medicine lies at a distance, underlined in our EH interview with Professor Michel Claudon, head of Radiology at the Regional University Hospital, Nancy, France, whose particular interest is ultrasound. Advances in IT and telecommunications have driven expert healthcare provision even into the most remote rural areas – underlined by this notable test in ultrasound

The Melody System is the world's first remote ultrasound imaging system. Produced by French company AdEchoTech, and developed by radiologists for radiologists, the system has evolved to meet the real needs of an ultrasound examination. Recognising that the necessary precision would be impossible using only a voice-controlled robot, the system incorporates the most recent audio-visual teleconference technology with advanced remote robotics similar to those used in space exploration.

The lead radiologist controls the entire examination from a central workstation, where the video link enables the patient, operator and ultrasound images to be seen on high-resolution computer screens throughout the examination. The highly sensitive audio-link also enables the expert radiologist to instruct the operator and discuss with the patient throughout the procedure.

However, most importantly, it is the use of a 'dummy' probe by the expert that drives the robot and therefore, ensures exam quality. While watching the images, the expert moves the dummy probe as they would if physically at the patient's side.

Currently used primarily for abdominal ultrasound examinations, the lead radiologist has complete control over the set-up parameters of the images, such as gain control, depth control, frequency change and activation of various ultrasound modes, such as Colour Doppler and Pulse Wave Doppler.



An examination can be carried out remotely using a 'dummy' probe that drives the robot. The operators, like the one here, said they quickly adapted to using Melody system

Is the system as good as it seems? Claudon's team organised a test to find out. The Melody system was set-up in the Lunéville Hospital centre, over 30 km away from the specialist centre in Nancy.

The equipment was very easy to set-up – within a day it was completely operational in the Lunéville ultrasound room with the secure audio-video link picking-up the images in Nancy.

Over the next three days approximately 30 different abdominal ultrasound examinations were performed with the system. Following instructions from Nancy, the patients placed themselves on the couch and operator positioned the robot over their body and applied gel. The probe on the robot, inclined at 45° then followed the movements of the expert's dummy probe to perform the examination.

The team were quite surprised at how quickly they adapted to using the system, within two-three examinations 'to use a dummy probe honestly became completely natural'. Also the images provided are completely compatible with the hospital's PACS, so they could be automatically archived for future reference.

What about the patient? In this series of tests, patients were completely relaxed and compliant and had absolutely no difficulty with the concept of having the specialist at a distance. For them the end result of the examination is the same but without the loss of time and other potential difficulties of having to travel to the specialist centre.

Are there limitations? The system is as good as the internet connection for the specialist to feel that they are present at the examination. It has to be performed in real time, with no pauses and screen break-up. While fibre-optic cable will produce the best results, for longer distances satellite connections may add up to a millisecond of difference, which nevertheless should be imperceptible to the radiologists concerned.

There is also the ergonomic question of probe depth because the pressure exerted by the robotically controlled probe is not the exact equivalent of the radiologist's hand but, as with robotic surgery, future developments and greater use of such systems will overcome.

The team in Nancy are unanimous in praising the system and can see advantages far outweigh the minor disadvantages. They consider it could enable specialist radiologists to intervene earlier in diagnoses, reduce travel for frail patients, training of junior radiologists and a host of other applications.

* European Hospital would like to acknowledge the help of Dr Alix Martin-Betaux, Dr Frédéric LeFevre (CHRU Nancy) and Dr Eric LeFebvre (AdEchoTec) in producing this article.

Michel Claudon is Professor of Radiology and Head of Department at the Children's Hospital of the University of Nancy. In addition to his presidency of the WFUMB he is current president of the French Academy Council of Radiology and President Elect of the European Society of Urogenital Radiology. His medical interests include uro-radiology, technical advances in ultrasound, such as contrast and volumetric ultrasound and paediatric radiology. The professor has published 133 peer reviewed articles and has been an invited contributor to more than 100 conferences.

Sleep deprivation

Too little sleep takes a toll on your heart, according to a new study presented at the annual meeting of the RSNA. 'For the first time, we have shown that short-term sleep deprivation in the context of 24-hour shifts can lead to an increase in cardiac contractility, blood pressure and heart rate,' said study author Daniel Kuetting MD, Department of Diagnostic and Interventional Radiology, University of Bonn Germany.

For the study, Kuetting and colleagues recruited 20 healthy radiologists with a mean age of 31.6 years. They underwent cardiovascular magnetic resonance (CMR) imaging. The researchers also collected blood and urine samples from the participants and measured blood pressure and heart rate.

Following short-term sleep deprivation, the participants showed significant increases in mean peak systolic strain (pre = -21.9; post = -23.4), systolic (112.8; 118.5) and diastolic (62.9; 69.2) blood pressure and heart rate (63.0; 68.9). They also had significant increases in levels of thyroid stimulating hormone (TSH), thyroid hormones FT3 and FT4, and cortisol, a hormone released by the body in response to stress.

When misdirected antibodies

No case for a psychiatrist's

Up to ten years ago only a handful of antibodies that could be detected in the blood were known to neurology. Patients had inflammatory changes in the brain or spinal cord and also malignant tumours. When an antibody was detected this automatically triggered the search for a tumour. Usually, patients' neurological symptoms improved once the tumour was removed.

In 2005, the Catalan neurologist Dr Josep Dalmau, working at the University of Pennsylvania in Philadelphia, was the first researcher to describe new antibodies found in liquor from young women suffering encephalitis, but not necessarily also from uncontrolled tissue growth. This was the starting signal for the discovery of new antibodies, a process that is still not complete.

GENERATE – German Network for Research on Autoimmune Encephalitis
Founded in 2014, the network is entirely initiated by 'investigators' and is supported by 63 centres in Germany, aiming to help patients. Next to information from patients and doctors the main objective is to create a register; so far, this contains 570 pseudonymised sets of data. They facilitate internationally comparable research into the disease.
http://www.generate-net.de/

In Germany the Institute for Clinical Chemistry at the University Hospital Schleswig Holstein is pursuing the diagnosis of, and research into, these antibodies. In our European Hospital interview with Professor Klaus-Peter Wandinger and PD Dr Frank Leypoldt, neurologists and trained/trainee laboratory medics, we asked how Dalmau discovered the new antibodies.

Wandinger: 'Professor Dalmau carried out research in the field of neuro-oncology in the US for a long time and collected and examined a lot of liquor and serum. He found N-Methyl-D-Aspartate-Receptor (NMDAR) antibodies in around 100 patients, who all had similar clinical symptoms and responded to immunosuppressive treatment. These were mainly young women aged between 20 and 40, who initially displayed psychiatric symptoms.

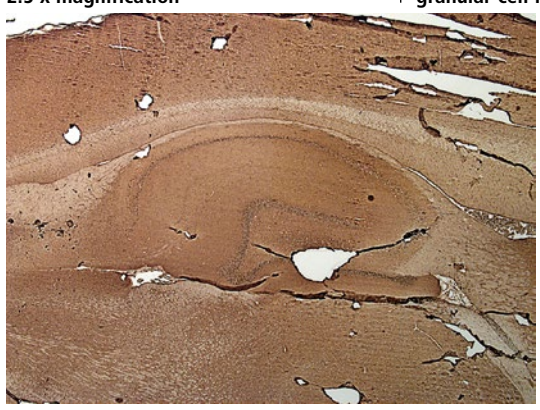
'The clinical picture usually started with the patients hearing voices or experiencing hallucinations, similar to schizophrenia. They then also suffered from epileptic fits, which were so severe that their breathing was affected to such an extent that they had to be treated in intensive care. It was a severe clinical picture, which was life threatening in around 20% of patients but which, up to that point, could not be diagnosed.'

Following medical studies at the University of Lübeck **Professor Klaus-Peter Wandinger MD** became a researcher in the Neuroimmunology Department at the National Institute of Neurological Disorders and Stroke (NINDS) in Bethesda/USA. In 2000 he became a researcher under Professor Einhäupl in the Neurology Department at the Charité Clinic. Three years later he wrote his habilitation on a neuroimmunology topic. He was involved in the development of laboratory procedures at Euroimmun and, since 2013, has been Deputy Director of the Institute of Clinical Chemistry, Campus Lübeck, University Hospital Schleswig-Holstein (UKSH).

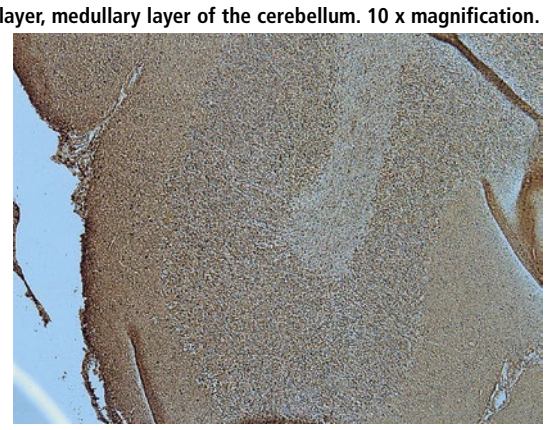
What are NMDAR antibodies and how do they trigger these symptoms?

Leypoldt: The NMDAR antibodies are a subspecies of glutamate receptors. Glutamate is a messenger substance in the brain that transmits impulses from receptor to receptor. The antibodies that normally fight

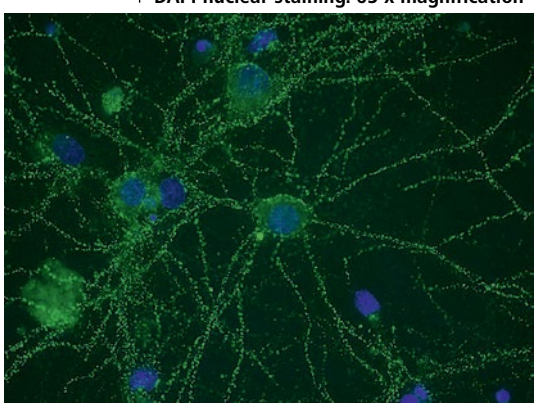
Example of neuronal autoantibodies, in this case directed against Neurofascin 155. Immunohistochemistry with specially prepared rat brain tissue samples. Areas marked in brown are identified by human IgG from patient serum. The hippocampal formation is visible in the central part. 2.5 x magnification



Immunohistochemistry with visualisation of anti-neuronal antibodies against the cerebellum on specially fixed rat brain tissue samples, in this case directed against glutamate receptors type AMPA. Areas marked in brown are identified by human IgG from the patient serum. From outside to inside: molecular cell layer, Purkinje cell layer, granular cell layer, medullary layer of the cerebellum. 10 x magnification.



Indirect immunofluorescence with patient liquor on specially prepared, non-fixed, non-permeabilised, embryonic hippocampal primary culture neurons. The binding of human IgG to the surface is marked in green. Green dots correspond with synaptic clusters of the target antigen Iglon5. Blue corresponds with DAPI nuclear staining. 63 x magnification

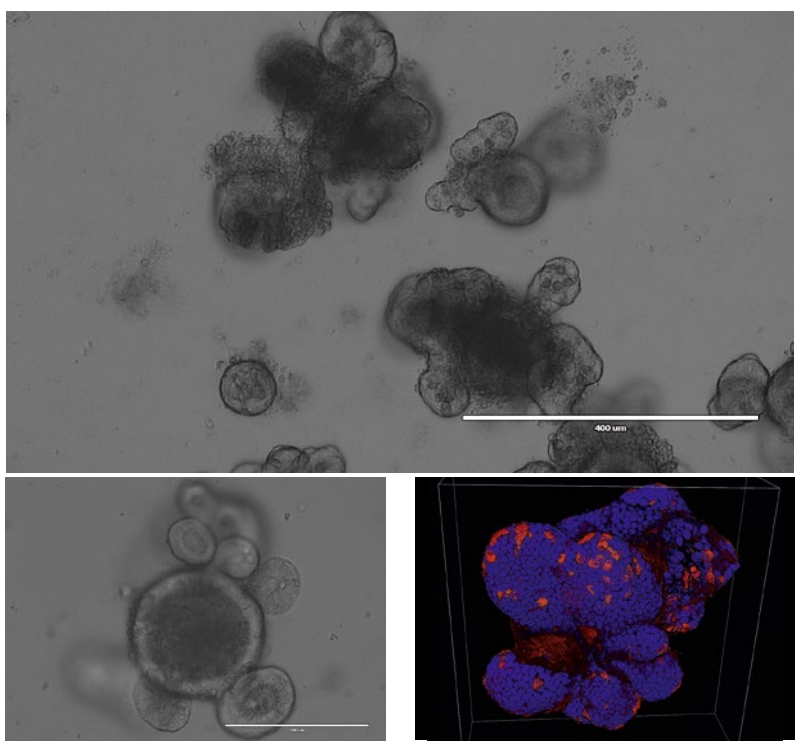


Medication testing in real life conditions becomes possible

The birth of the amazing organoids

Professor Hans Clevers, researcher and group leader at the Hubrecht Institute in Utrecht, the Netherlands, invented the organoids, a ground-breaking new technique to grow new 'organs' and to test medication. This year, his work was rewarded in the form of the prestigious Korber European Science Prize*, presented in Hamburg. At the Heinrich F C Behr-Symposium he discussed organoids and the individual therapy for colon cancer made possible by this significant development.

For years, Clevers has studied how cancer develops and what goes wrong at the DNA level. 'Until 2007 it was thought that bowels do not contain stem cells. We discovered that they do, and even more, that they divide themselves every day. To make that visible, we added the DNA of fireflies in the stem cells of mice. And what happens in mice, also works for people. This discovery was a real breakthrough and it was a race against time to be the first to come out with this study. We – mostly – won this race, but it was also worth a lot to see that other researchers, who were on the same track, confirmed our research.'



Together with the Royal Academy of Sciences, Hans Clevers founded the Hub to test the operation and effectiveness of drugs on a large scale, using organoids. 'We need human material to grow organoids,' he explained. 'Because of this non-profit organisation, people find it less difficult to donate cells for research.'

The development of organoids

The discovery of stem cells in the intestines led to further investigation and, within two years, Clevers and team managed to grow a small intestine in a petri dish from a stem cell. The result is a new standard for the unlimited reproduction of adult stem cells, from which organs can grow in mini-size. Moreover, these 'organoids' contain all the cells that behave just as they do in the intestines, meaning that medication can be tested in real-life conditions.

Personal treatment method

Using organoids also leads to answers to questions such as how do cells work together; what they need from each other; what goes wrong to cause a particular disease, and especially how it can be solved. 'With these so-called 'Tumoroid' studies, research is carried out on the patient's disease. You harvest a few cells from the patient, out of which the organoids can grow.

'This is far less stressful than several physical examinations. The result is that you can prove which medication will be most effective for this patient in order to provide him with personal treatment.'

Cystic fibrosis variants

Clevers, in close cooperation with Kors van der Ent and Jeffrey Beekman, from the Wilhelmina Children's Hospital, proved the benefits of this technique. A Dutch patient named Fabian, aged 18 years, suffers a rare form of cystic fibrosis. 'The medicine Ivacaftor was tested for people with cystic fibrosis who had emerged from the same DNA error.

Fabian was not eligible for the drug because it was not tested for the gene that causes his form of CF. With organoids, we showed that Ivacaftor would also work in him. So he was given the medicine after all and is now doing great.'

Dilemma and global training

However, the use of organoids also leads to a dilemma. 'The cost of medications is high,' Clevers pointed out. 'You can still say "yes" if you can prove that medication will indeed help, but we can also predict with certainty when it does not. So do we have to refuse a medicine that people are entitled to have?' Additionally, current regulations regarding the authorisation of new drugs are not yet adapted to the recent developments. 'Therefore, we unfortunately cannot make any statements yet for colon cancer,' Clevers explained. 'The regulations also demand more testing on animals, whilst the use of organoids can diminish the use of animals in laboratories.'

Clevers is training lab staff worldwide in growing organoids. 'In Hong Kong, for instance, influenza viruses were tested on pieces of lung removed during lung surgery. They needed to work very fast, because those pieces only remain good for four days. We have trained researchers from Hong Kong in our lab in Utrecht and now the technique is being applied there.

The Future

Clevers has not finished his studies. 'The heart is still a virgin territory when it comes to the question of whether that organ has stem cells. In addition, the research into the application of organoids is still in progress. Yes, we can grow miniature organs and implant them in animals, but is that safe? Suppose you grow mini organ stem cells from a donor bank. Will you give the patient a new liver, but also perhaps a disease? Another step is the development of tailor-made drugs by pharmaceutical companies.'

His big dream, however, is the emergence of a liver bank, containing 'freezers with pieces of liver

s cause neurological diseases

couch

PD Dr Frank Leypoldt is currently training as a specialist in laboratory medicine at the Institute for Clinical Chemistry at UKSH. He also heads the neuroimmunological out-patient department at the UKSH Campus Kiel. A qualified neurologist, he gained his doctorate at the University Hospital Hamburg-Eppendorf, where he also completed a postgraduate course in molecular biology. He worked in Hamburg as a post-doc fellow and, between late 2012 and 2014, in Barcelona under Professor Josep Dalmau. He has been employed at the UKSH since 2014 and wrote his habilitation in 2015.

foreign cells in the body for reasons still unknown, bind to the NMDA receptors and block the transmission by the messenger substance. Communication between the nerve cells is impaired, which leads to psychiatric and neurological symptoms.

'In Dalmau's study, up to 40% of patients, amongst them many female Afro-Americans, had ovarian teratoma i.e. a benign ovarian tumour; in a German study cohort of patients, 25% were affected. As germ cell tumours also develop nerve cells it's assumed that these trigger the autoimmune reaction against the NMDA receptor.

What happens when the anti-NMDA receptor encephalitis is not diagnosed in time?

Wandinger: 'This is a real problem. We are currently raising awareness of this through the German Network for Research on Autoimmune Encephalitis (GENERATE). In the worst instance, such as the case of a child in Northern Germany, encephalitis is diagnosed through an examination of the liquor, but the laboratory does not find any pathogens. Without the test for neuronal antibodies and the respective immunotherapy the patient's condition did not improve and he was on the brink of being transferred to a facility for the disabled. It was only after a consultant in the rehabilitation clinic ordered an antibody examination that the patient received the appropriate help, and he is now able to lead an independent and self-sufficient life again.

'Thankfully, many more neurologists are now aware of this disease and there are test systems used in laboratories worldwide for the detection of the antibodies. If no diagnosis is made the disease can also have a fatal outcome.'

What is the incidence of this disease?

Leypoldt: 'It is a rare disease and we are trying to determine exact epidemiological data through the register of the national network. Current estimates stand at around one case per one million people a year. However, autoimmune encephalitis is more frequent than all types of encephalitides caused by pathogens such as Herpes Simplex Encephalitis.'

Which examinations do you perform at the institute?

Wandinger: Over the last ten years a further 12 antibodies have been

Continued on page 12

Professor Hans Clevers MD gained his medical degree in 1984 and a PhD in 1985 at the University of Utrecht, the Netherlands. He carried out his post-doctoral work (1986-1989) with Dr Cox Terhorst at the Dana-Farber Cancer Institute, Harvard University, Boston. From 1991-2002 Clevers was Professor of Immunology at the University Utrecht and, since 2002, Professor in Molecular Genetics. Between 2002-2012 he directed the Hubrecht Institute in Utrecht. Additionally, between 2012-2015 presided over the Royal Netherlands Academy of Arts and Sciences (KNAW). Since June 2015 he has directed research at the Princess Maxima Centre for paediatric oncology.

that completely match the patient's tissue and, further into the future, banks with other cultured organs. Research goes much slower than you think, but currently ten times faster than anything we've ever experienced. So when I think of it, we will have that liver bank between now and ten years.'

* Awarded annually, the Korber Prize, worth €750,000, is one of the highest awards in medical world. With physics and biomedical sciences alternating every other year.

"Parsimony is the key in genetic data study"

Simplifying what is complex

Genetics stepping ahead as Spain-based researchers develop biomedical robots that can help in the study of rare diseases, neurodegenerative disorders and cancer, as well as the creation of orphan drugs

Report: Mélisande Rouger

Predicting disease development and anticipating adequate treatment may appear to be as uncertain as gazing into a crystal ball. But, what if there was a way to sort out and classify the myriad available genetic information to help doctors to do so?

A multidisciplinary team from Oviedo University is beginning to demonstrate that possibility by using biomedical robots that can adapt and improve predictions as they unravel phenotype – how genetic information expresses itself in a given environment.

'Searching for classifications that can optimally explain gene expression is a little bit like trying to open a safe deposit box with multiple combinations. We are working with 50,000 genetic probes in cohorts of 100 or 200 patients at a time; this means we are dealing with an extremely high level of indetermination.

'We need tools that take into account the degree of uncertainty contained in phenotype prediction and understand that genetic networks have their own structure,' explained Professor Juan Luis Fernández-Martinez, Head of Inverted Problems at the Mathematics Department in Oviedo University.

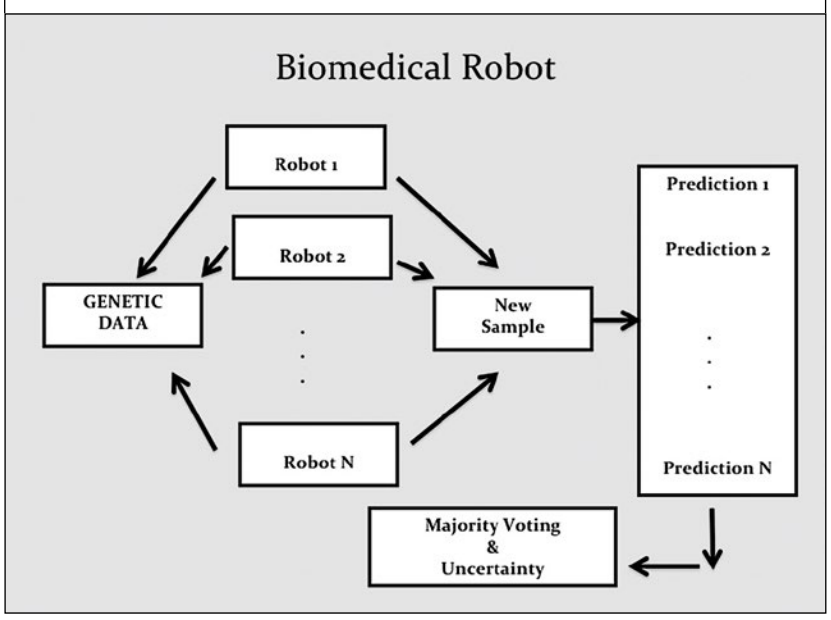
Combining knowledge from applied mathematics, statistics and computational science, since 2010 Fernández-Martinez and team have been designing biomedical robots with Biomodels, a company headed by Dr Steve Sonis from Harvard University and Brigham and Women Hospital in Boston.

Their robots are able to learn from complex data sets and help doctors make decisions and plan personalised treatment according to a patient's needs; in a word, they enable personalised medicine.

The principle behind designing such machines is simpler than one might have thought. 'People believed they needed highly complex computers to treat so much data, but we actually did it with a pretty simple model. Basically, we applied the concept of parsimony. Uncertainty comes from ambiguity in knowledge, so it's interesting to look at things through that angle and simplify what is complex,' Fernández added.

The engineer and his colleagues believe the machines will not only help in the study of rare and neurodegenerative disease and cancer, but also in designing orphan drugs and new treatments, and tailoring therapy to each patient. The team has just published a study in the *Journal of Computational Biology*, in which they show robotic potential in chronic lymphocytic leukaemia, inclusion body myositis and amyotrophic lateral sclerosis.

Professor Fernández-Martinez (left) with Dr Enrique J Andrés Galiana outside the Geology Department at Oviedo University.



In leukaemia, the researchers have highlighted the relevance of Lipoprotein lipase, an enzyme that decomposes triglycerides in free fatty acids and glycerol. The team has also discovered the importance of certain genes and how viruses and bacteria influence the genesis of myositis, an autoimmune disease affecting the muscular system, by showing how the immune system mistakes the organism's proteins with those of the invader.

Biomedical robots have also been able to underline the importance of caspases, a group of proteins controlling programmed cell death and which have been related to mutations in gene SOD1, a cause for amyotrophic lateral sclerosis.

All these findings still need clinical validation, Fernández-Martinez stressed.

Meanwhile, the Oviedo team has developed tools that can help differentiate between genes called headers, which are responsible for most of the phenotype, and helpers, adjuvant genes that bring further detailed information on discrimination. Researchers have applied this method to a toxicity study and will publish results soon on Parkinson and Alzheimer's disease from the so-called Finisterrae project (http://www.slideshare.net/ifalberti/effective-analysis-of-biomedical-big-data-for-the-optimisation-of-drugs-for-rare-and-neurodegenerative-diseases-and-cancer).

The Oviedo researchers also recently published a paper questioning most of what has been said so far on microarray preprocessing techniques by showing their impact in biological pathways (Impact of Microarray Pre-processing Techniques in Unravelling Biological Pathways, Journal of Computational Biology, http://online.liebertpub.com/doi/abs/10.1089/cmb.2016.0042).

'Genetics is still an understudied field and gene function is often misunderstood. Our long-term goal is to make a genetic test as common as a blood test,' Fernández-Martinez said. 'We will multiply cooperation projects with the medical field to do so.'

Trained as a petroleum engineer in Paris (1988) and London (1989), and after years as an IT software engineer in France, in 1994 **Juan Luis Fernández-Martínez** gained a PhD in mining engineering from the University of Oviedo, in Spain. He joined the university's mathematics department and became Professor of applied mathematics. During 2008-2010 he was a visiting and research professor at UC Berkeley-Lawrence Berkeley Laboratories and Stanford University. His expertise includes cooperative global optimisation methods, with applications in oil and gas, biometry, finance and biomedicine – in which he aims to design biomedical robots in translational medicine for diagnosis, prognosis, and treatment optimisation. The Finisterrae project particularly aims to find effective solutions for rare and neurodegenerative diseases, as well as various types of cancer.

Refined capillary blood collection

Small tubes, great impact

The capillary blood collection system not only benefits geriatric patients, or those who need regular blood sampling, but also burns victims and others, including the youngest patients. All need a gentle approach. To that end, Austrian firm Greiner Bio-One has developed and optimised its MiniCollect system.

The MiniCollect capillary blood collection system

No more tubes and funnels

The cumbersome process of transferring the drop of blood using capillary tubes or funnels is in the past, thanks to this system because the blood collection scoop is integrated into the wide tube opening. 'The sample comes into contact with the additive immediately,' the manufacturer reports. 'The caps are completely sealed, meet the highest standards and can easily be sent via pneumatic dispatch or other transport systems without losing any sample material.'

Carrier tubes and combined filling volumes simplify use

'For centrifugation, the MiniCollect tubes can be inserted into a premium carrier tube using a simple rotational movement. When combined, the dimensions correspond to a standard 13 x 75 mm tube format and can easily be placed in a standard rack or standard centrifuge.'

Two easily visible filling marks on the tube provide greater flexibility for use.

The new MiniCollect capillary blood collection system went on show at Medica 2016

No case for a psychiatrist's couch

Continued from page 11

identified, many of those by Josep Dalmau, but also by Angela Vincent, in Oxford, who heads up the second largest working group on this topic. Neurologists can indicate a suspected anti-immune disease and also any clinical details on our test request form. We then use the procedures we've developed to test for the known neuronal antibodies, and also for antibodies as yet unknown, using further tests from our research laboratory that were developed in close cooperation with Professor Dalmau and which are not available to buy.

'We not only do this for hospitals in all of the German speaking countries but we also work with laboratories in Spain, the USA and Australia. Our dual qualification is unique. I am already a qualified specialist for laboratory medicine and Dr Leypoldt will soon qualify. When a positive result is confirmed we are well qualified to advise doctors on treatment.

'The clinical pictures of autoimmune diseases are not that well known outside of centres for maximum care, and colleagues are grateful for our guidance.'

Might more antibodies be discovered?

Leypoldt: 'It is to be assumed that more will be found as there is a vast number of potential target proteins within the nervous system. Theoretically, each protein can trigger an auto immune reaction in the body, especially when it's located on the cell surfaces where antibodies have good access. Some people most probably have a genetic predisposition.

'For now, the large groups, the most common autoantibodies, have been described with the laboratory procedures currently available. But the research continues for seronegative, i.e. antibody negative autoimmune encephalitides, for example. If no antibodies can be detected it doesn't necessarily mean that they don't exist.

'One of Dalmau's most important findings was the development of new laboratory procedures that can be used to identify a whole group of diseases through defined antibodies, i.e. patients who we had previously only perceived as suffering from encephalitis.

'There are biomarkers for specific groups of diseases that are very similar and treatable. Following this advance into new dimensions it is likely that further steps will be made to identify and treat diseases not yet classified.'

Bringing a new technology over the translation bridge is not so easy

Fusing microscopy and mass spectrometry

Report: Lisa Chamoff

Pathology does not appear to have much in common with satellites, but the concept that satellites combine spatial resolution and image quality will be the future of disease diagnosis, according to researchers.

Scientists at Vanderbilt University, Nashville, Tennessee, are combining microscopy and mass spectrometry, using mathematical regression analysis to take advantage of each mobility's strength.

'In a satellite imaging process a black and white picture of the ground is taken because black and white cameras have high spatial resolution,' explains Richard Caprioli, director of the Mass Spectrometry Research Centre at Vanderbilt University School of Medicine. 'A colour camera also takes pictures at the same time. The colour camera has millions of colors, but the resolution is lower. A process called image fusion takes the best of both worlds and combines them mathematically to produce an image that has both high resolution and lots of colours.'

Whilst a microscope gets a much higher resolution, it provides no molecular data. Mass spectrometry, on the other hand, is used to measure the molecular characteristics of a disease that are present in the patient's sample. 'Instead of just one protein, we are looking at a whole suite of proteins, which we call a disease signature,' Caprioli explains. 'Now, when you put together high resolution microscopy and the high molecular dimensionality of mass spectrometry, you produce high-resolution molecular spectroscopy images.'

Caprioli's team has been studying image fusion to diagnose melanomas, prostate cancer and breast cancer. They are currently in the discovery process, looking at how image fusion differentiates between two stages of a cancer among a couple of hundred patients. The researchers look for a list of proteins that come with the specific disease stage.

Caprioli believes that image fusion for pathology will be used in the next two to three years for the 'most important cases where the pathologists don't have the tools for such comprehensive molecular interrogation of tissue.'

In a paper published last year in the journal *Nature Methods*, Caprioli's team used image fusion to study protein, peptide, lipid, small metabolite and drug distributions in tissue.

'Image fusion enables a new multimodality paradigm for tissue exploration whereby mining relationships between different imaging sensors yields novel imaging modalities that combine and surpass what can be gleaned from the individual technologies alone,' the authors wrote.

A similar technology has been under development at the Oak Ridge National Laboratory (ORNL) in Oak Ridge, Tennessee, although there it is used for materials characterisation rather than disease progression. At ORNL, the two imaging modalities are being put together mechanically, while researchers at Vanderbilt are using lasers.

The challenge will come in making pathologists aware of the new technology when it will be ready to be put to use and engaging them in discussion. 'Bringing a new technology over the translation bridge is not as easy as many people think, Caprioli comments.The College of American Pathologists has identified imaging mass spectrometry as an important technology and has begun its certification process. Additionally, this will eventually need clearance from the USA's Food and Drug Administration.

'I believe that, in the coming years, all diagnoses will be done this way, because it makes sense,' Caprioli confirms. 'You're looking at what is wrong with the patient directly and not just picking out a few surrogate markers for the disease. Pathologists have tools that they use today. We are offering a new set of tools that have high molecular dimensionality.'

Richard Caprioli directs the Mass Spectrometry Research Centre at Vanderbilt University School of Medicine

Integrated immunoassay analyser handles over 400 tests per hour

A swift new lab automation system

'Every single hour, more than 200,000 people worldwide are being diagnosed or treated with our devices,' Michael Reitermann, COO of Siemens Healthineers, proudly reports. No reason, however, for Siemens to rest on its laurels. Quite the contrary: the company continues to drive innovation. Case in point is Atellica Solution, the firm's most recent lab automation system, unveiled at this year's congress of the American Association for Clinical Chemistry (AACC), in Philadelphia. 'With Atellica we created something entirely new in the lab world – something we had been working on for quite some time,' explains Franz Walt, President of Laboratory Diagnostics at Siemens Healthineers

'We put a lot of detail work into the Atellica system; it not only contains a high degree of Siemens internal engineering know-how but also many insights culled from comprehensive customer surveys,' Franz Walt confirms. For years, the firm has talked with customers, asking precise, concrete questions in order to collect information that would enable its engineers to tailor a system to customers' needs.

Completely developed in-house

The result is a solution that features Atellica Magline, a bi-directional, magnetic sample-transport technology that is ten times faster than conventional technologies, Siemens reports. 'What's so incredible about this conveyor is the technology behind it – it is based on magnetic levitation technology with very little mechanical contact which in turn means hardly any wear and tear and extremely low maintenance,' Walt explains.

But innovative transport is not the only innovation Atellica Solution has to offer, the manufacturer points out. 'The integrated immunoassay analyser delivers the industry's highest productivity per square metre – more than 400 tests per hour. A multi-camera vision system and intelligent sample routing enable independent control over every sample, from routine to STATs.'

For comprehensive multidisciplinary use Atellica can also be connected to Aptio Automation. Moreover, the solution can handle more than 30 sample container types, including paediatric and special containers.

'Atellica is unique as we gave it a modular design which enables the customer to choose almost any conceivable configuration. The entire system is scalable and offers more than 300 customisable configurations,' Walt says, obviously proud of his new lab champion. The solution can be used as a standalone system or connected to automation, including L-shaped, U-shaped or linear formations and up to ten components can be combined.

'We succeeded in designing an innovation which allows our customers to achieve better clinical as well as more relevant business results without having to spend more time on lab tests,' he adds.

A bi-directional, magnetic sample-transport technology, Attelica Magline, is reported to be ten times faster than conventional technologies

Innovations based on trends

'With this development we clearly focus on customers' needs – the beginning of an exciting strategy Siemens Healthineers will follow – a strategy we will continue to invest in,' says Michael Reitermann charting the future course. 'We will continue to optimise processes for customers and will focus on customers – which is what, in the end, they expect.'

In global healthcare developments, Reitermann says, three major trends can be seen: 'Firstly, there's a clear trend towards consolidation among service providers. Secondly, there's a trend towards industrialisation in the healthcare systems, which are increasingly shaped by an ever-stronger focus on efficiency. The third trend concerns the reimbursement system, which moves away from an input-based to a value-based or output-based system that focuses on the real value of the services rendered.'

Michael Reitermann: 'We understand these trends and their effects on our customers. Therefore we orient our innovation efforts towards the principle 'Improve Outcomes – Reduce Costs.' In order to be able to deliver on this promise, Siemens Healthineers identified Molecular Diagnostics, Advanced Therapies and Services as growth areas.In late July, the US Food & Drug Administration (FDA) officially accepted Siemens' submission of Atellica Solution for review. This is another milestone in the new direction the laboratory segment is taking and the starting signal for more innovations by Siemens Healthineers, the firm points out. As COO Reitermann reveals: 'We have several other innovative developments for the new Atellica product family in our R&D pipeline.'

Michael Reitermann is Chief Operating Officer (COO) with Siemens Healthineers. A qualified industrial engineer, also with MBA degree, he joined Siemens in 1990. Having held positions in different departments and locations, he knows the company inside out.

Swiss-born **Franz Walt** became President of Laboratory Diagnostics of Siemens Healthineers in 2014. He delivers 27 years of management experience within two leading healthcare companies – including Siemens Healthineers – to his current position.

Diagnosing Zika virus infection

Commercial blood test proves reliable

The Society for Virology (GfV) which promotes virology through the increase and exchange of research within German speaking countries, as well as via cooperation with other scientific societies, announced this year that a new test can unambiguously confirm the diagnosis of a Zika virus infection – leading to fast diagnosis and identification of an infection. The diagnosis of pregnant travellers worried a Zika infection upon their return home was cited as one example. Waiting for a diagnosis is just a few hours.

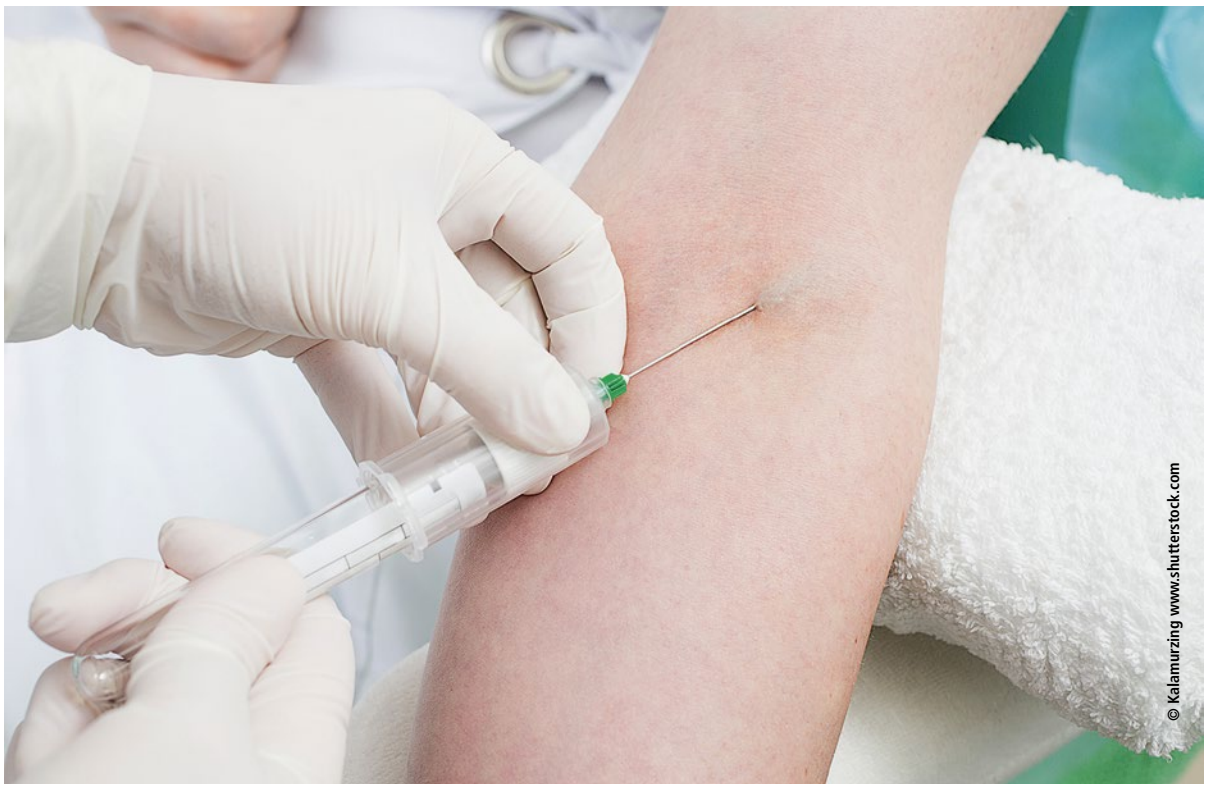
Commercial blood test

Researchers at the University Hospital, Freiburg and at the Bernhard Nocht Institute for Tropical Medicine have now substantiated the use of a commercial blood test for antibodies. 'This test detects Zika virus antibodies reliably and, unlike other procedures, shows no cross reactivity with other, related viruses," confirmed Dr Daniela Huzly, head of Diagnostics at the Institute of Virology in Freiburg. Professor Thomas Mertens, President of the Society for Virology, added: 'The availability of a reliable and fast test for the specific and sensitive detection of Zika virus antibodies is a great relief for those who may be infected as well as for doctors.'

A small window of time

In a patient with an acute infection the Zika virus has generally been confirmed via direct virus detection, a so-called PCR test. However, diagnosis is only possible during a small window of time and only works during the first few days of an infection. Most patients therefore require a serological examination, i.e. a test for antibodies.

One problem with this is that the antibodies developed by the body against the Zika virus show a distinct cross reactivity with antibodies against related viruses in most of the previously used blood tests. Thus a test reacts positive when antibodies against other viruses circulate in the blood, such as those against FSME, Yellow fever or Dengue fever. This is a problem not only for those already infected but also those previously vaccinated against one of these viruses.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Ascertaining whether a patient really is infected with the Zika virus therefore required further, extensive tests that can only be carried out in a few specialist laboratories. The new test, however, does not require extensive diagnostics and can be carried out in any laboratory that routinely tests for antibodies.

Also test men with pregnant wives

The Society for Virology and the Bernhard Nocht Institute for Tropical Medicine recommend confirming a potential Zika virus infection not only for pregnant travellers returning from locations where the Zika virus has spread, but also for men who have spent time in those areas and have pregnant partners. In both cases testing is also recommended when no symptoms or illness are present.

Returning travellers who had symptoms typical of a Zika virus infection, such as fever, headache, lethargy, muscle and joint pains, rash, conjunctivitis, can also be tested to check whether they are infected, even when symptoms may have been mild.

Source: Society for Virology, http://g-f-v-org/newsletter

Moving through the R&D pipeline

A pan-cancer screening test

Cancer blood tests might become available in the near future. Last January Illumina, Inc., a USA-based firm, announced the creation of GRAIL, a new firm aiming to enable cancer screening from a simple test measuring nucleic acids circulating in blood.

The earliest cancer detection increases long-term survival. The successful development of a pan-cancer screening test for asymptomatic individuals could, effectively, diminish global cancer mortality.

Grail, now as a separate company, with majority owned by Illumina, is initially funded by over $100 million from Illumina and ARCH Venture Partners, with participating investments from Bezos Expeditions, Bill Gates and Sutter Hill Ventures. 'The holy grail in oncology has been the search for biomarkers that could reliably signal the presence of cancer at an early stage,' said Richard Klausner MD, formerly Illumina Chief Medical Officer and NCI Director, and a Grail Director. 'Illumina's sequencing technology now allows the detection of circulating nucleic acids originating in the cancer cells themselves, a superior approach that provides a direct rather than surrogate measurement.'

Grail has secured the counsel of a world-class set of industry and cancer experts for the company's advisory board, including Klausner, Dr Jose Baselga, Physician In Chief at Memorial Sloan Kettering and President of the American Association of Cancer Research; Dr Brian Druker, Director, OHSU Knight Cancer Institute; Mostafa Ronaghi, Chief Technology Officer at Illumina; Don Berry, Professor at MD Anderson Cancer Center; Timothy Church, Professor at the University of Minnesota School of Public Health and Charles Swanton, Group Leader at the Francis Crick Institute.

The company will initially have a five-member Board of Directors, including Jay Flatley, William Rastetter (Chairman of Illumina), Richard Klausner, Robert Nelsen, and the CEO – former senior Google executive Jeff Huber.

Huber, who has now led Grail since last February said, in a US magazine interview for Forbes at the time of his appointment, that he took on this role largely due to the death of his wife, Laura, from colon cancer in late 2015.

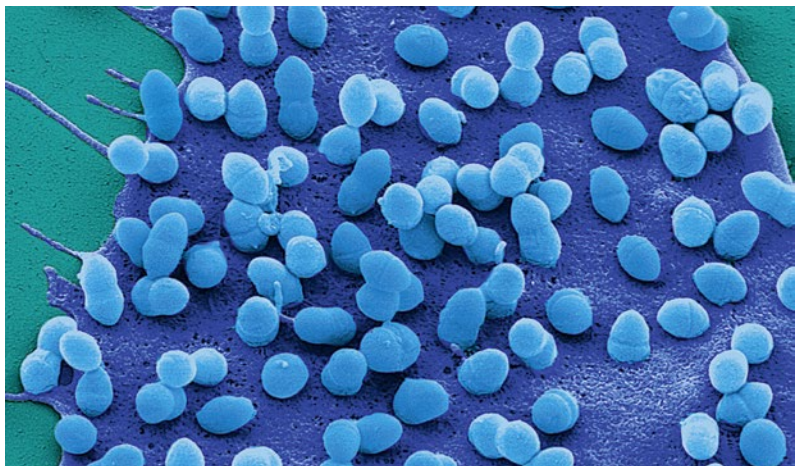
Mathematical model elucidates immune system reactions

Seeking the role of messenger substances in infections

Using computer-based simulations and mouse experiments, researchers at the Helmholtz Centre for Infection Research (HZI) in Braunschweig and at the Otto von Guericke University Magdeburg (OVGU), have disentangled the effects of pro-inflammatory signalling molecules on the post-influenza susceptibility to pneumococcal co-infection.

A body infected by the influenza virus is particularly susceptible to other pathogens. Bacteria like Streptococcus pneumoniae, i.e. the pathogen causing pneumonia, find it easy to attack an influenza-modulated immune system and to spread widely. This can even be fatal in some cases. The reasons for the bacterial growth in the presence of a co-infection by influenza virus and bacteria are still debatable. In the scope of an interdisciplinary project, the researchers discovered that the overproduction of a certain messenger might facilitate the proliferation of the bacteria in the presence of co-infection.

Up to 20,000 people succumb to the consequences of an influenza disease each year in Germany alone. However, in most cases it is not the influenza virus that leads to serious complications, but a second infection by bacteria acquired by the patient after the onset of influenza.



Streptococcus pneumoniae is a bacterium that can cause severe pneumonia and often attacks the body when it is weakened by influenza. Combined with influenza, this bacterial infection takes a particularly severe course and becomes life threatening. The processes, by means of which influenza affects the susceptibility to and the severity of bacterial infections, has not been well understood thus far.

Using an interdisciplinary approach, the research teams of Dunja Bruder, who heads the HZI's research group 'Immune Regulation', and a professor of infection immunology at the OVGU Magdeburg, and Dr Esteban A Hernandez-Vargas, who directs the 'Systems Medicine of Infectious Diseases' research group at the HZI, made a major contribution to solving this riddle.

The researchers jointly developed a project plan linking laboratory work with mice, infected concurrently with the influenza virus and Streptococcus pneumoniae, and computer-based modelling of the infection processes. 'Usually we simulate biological processes based on previously published data. Since we, as systems biologists at the HZI, work very closely with the infection researchers on-site, we could plan the infection experiments appropriately, so that the collected data would be ideally suited for mathematical modelling of the infection processes,' Esteban Hernandez-Vargas explains. In infection experiments, Bruder and her team were able to show that the number of macrophages – immune cells that eliminate pathogens – drops rapidly as early as 18 hours after co-infection of influenza-infected mice with the bacteria, and that the bacteria proliferate very rapidly.

When the systems biologists modelled the observed increase of the pneumococci and the simultaneous decrease of the immune cells through mathematical functions, they discovered that the two processes do not match exactly. 'This allowed us to deduce that the strong bacterial proliferation was not only due to the decrease in the number of macrophages. There had to be at least one more factor that played a role in this process,' says Bruder.

The scientists then looked at the release of various messenger substances that have important functions in the defence of bacterial infections. As before, exact time points for the collection of samples were defined in the investigation of these molecules to ensure the collected data would allow for the best-possible mathematical simulation of the on-going processes.

The scientists noted that the amounts of the messenger substances produced by the body in the presence of a co-infection were clearly larger than in the presence of a bacterial infection alone.

Hernandez-Vargas' team again entered the profiles of the numbers of bacteria, numbers of macrophages and the various messenger substances in his mathematical models. The best model was obtained with the measured interferon gamma data – another messenger substance – and a minor influence was also detected for interleukin 6 – both of which are molecules that are usually important for control of the immune defence in an infection.

'Due to the infection by the influenza viruses, the interferon gamma level is already high. Even more interferon gamma is produced if a second infection by pneumococci occurs. Based on our results, we are presuming that the macrophages can no longer effectively eliminate the bacteria because of this over-reaction of the immune system. It is known that their "elimination function" is impaired by excessive levels of interferon gamma,' Bruder explains.

Additionally, a computer simulation confirms this observation. If one withdraws the interferon gamma from the model, bacterial outgrowth may not be presented. Bruder's research team now plans to test the results of this simulation in laboratory experiments. 'If the experimental results are consistent with the results obtained by modelling, the mathematical model would give us a tool that allows us to predict the role of certain messenger substances in infection processes,' Hernandez-Vargas explains. 'As one of the benefits, laboratory experiments could be planned much better and the number of animal experiments could be reduced. Moreover, in the long term it might be possible to develop a therapy for co-infections that focuses on the interferon.'

Source: The Helmholtz Centre for Infection Research
Original publication: S. Duvigneau, N. Sharma-Chawla, A. Boianelli, S. Stegemann-Koniszewski, V. K. Nguyen, D. Bruder, and E. A. Hernandez-Vargas: Hierarchical effects of pro-inflammatory cytokines on the post-influenza susceptibility to pneumococcal coinfection. Scientific Reports 6 (2016), doi: 10.1038/srep37045; http://www.nature.com/articles/srep37045

Reliable and accurate results during lengthy pipetting sessions

Welcoming values in mechanical pipettes

With "Tacta" the pharmaceutical and laboratory equipment supplier Sartorius has recently launched a new mechanical pipette. Tacta has a perfectly balanced design that is easy, safe and comfortable to use. The pipettes meet the most demanding pipetting requirements, delivering consistent and accurate results time after time. Manufactured from carefully selected materials, each component is designed to meet the highest standards of comfort and reliability. The new pipettes are available in a range of volumes from 0.1 to 10,000 µl in single channel models, and from 0.5 to 300 µl in multichannel models.'

The extremely low pipetting and tip ejection forces reduce the risk of Work Related Upper Limb Disorder (WRULD), the firm points out. 'The unique handle and finger hook design let the pipette rest lightly in the user's hand, with no need to grip the handle tightly, providing reliable and accurate results during lengthy pipetting sessions.

'The new Sartorius Optiject, levered tip ejection technology, enables controlled and smooth tip ejection with minimum force. The Optiload feature, with spring-loaded tip cones in both single and multi-channel models, ensures tip loading with perfect sealing and minimal force.'

The new Optilock system provides flexible volume adjustment and locking functions, and prevents accidental volume changes during pipetting, Sartorius notes. 'Tacta has a large, clear 4-digit display, which makes the volume easy to read even when the pipette is at an angle. Furthermore, Tacta is very easy to adjust for a variety of liquids, using a simple adjustment key. An integrated adjustment functionality and scale show the degree of adjustment and, by noting this value for a specific liquid, the user can return to that setting any time.'

No tools are needed to disassemble the three parts, and the pipettes are reported to be particularly quick and easy to clean, and they can be autoclaved without disassembly, with high resistance to UV and chemicals exposure.

Safe-Cone Filters are available for all Tacta models with volumes of more than 10 µL, and the filter ejector enables easy removal of used or contaminated filters without human contact.

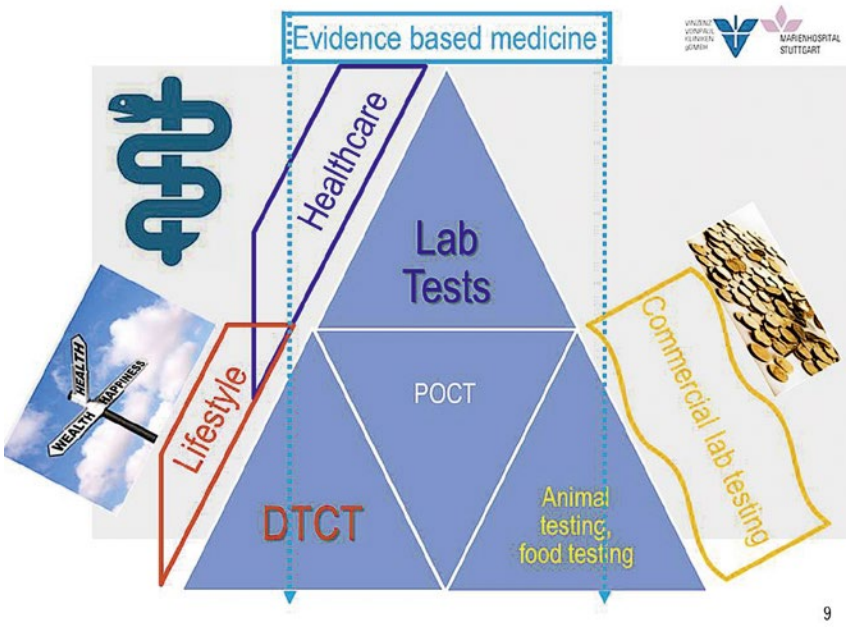
All Tacta pipettes are also fully compatible with original Sartorius Optifit and SafetySpace pipette tips.

More information: www.sartorius.com; www.passionforscience.com

How can some people thoughtlessly allow a genetic testing firm to use their genetic data?

The dangers of commercial direct-to-consumer tests

Lifestyle tests that pretend to be medical procedures are inherently problematic in terms of clinical, medical and privacy issues. Professor Matthias Orth, Medical Director of the Institute of Laboratory Medicine at Marienhospital Stuttgart, discussed 'Direct-to-consumer testing: The business of lifestyle tests' at a September congress in Copenhagen that focused on 'The benefits and challenges of point-of-care testing across the clinical spectrum'.



Integration of DTC testing

Direct-to-consumer testing (DCT), or direct access testing (DAT), are laboratory tests with results that go straight to the end customer or patient, explained Professor Matthias Orth. 'This includes tests ordered by a physician for medical purposes and clearly evidence-based tests, such as glucose monitoring or blood glucose sticks for diabetes patients. These exams are also POCTs – point-of-care tests. Furthermore, DTC tests encompass test strips, for example urine pregnancy tests or lactate tests in your gym.

'However, more recently a new generation of DCT tests has emerged: tests where the customer samples blood or DNA at home, mails the sample to the lab and then calls up results over the internet. According to the test providers, each sample is individually analysed, with the test pretending to be a medical lab service.'

Are these tests a problem for lab specialists and other healthcare professionals?

'In most countries the healthcare sector is highly regulated to protect the patient. In the USA, for example, the tests need FDA approval and labs must be certified by the Clinical Laboratory Improvement Amendments (CLIA). In Germany, we have a guideline issued by the German Physicians' Association for Quality Assurance of Lab Medical Exams. According to this, tests must offer a medical benefit; moreover only adequately qualified people can perform tests.

'There are also many more rules and regulations to protect the patient, such as privacy laws, regulations applying to healthcare professionals, the genetic diagnostics law and rules that govern physicians fees for services.

'All these – undoubtedly necessary and useful – laws and rules do not apply to lifestyle testing. Therefore we must now somehow define when the line between lifestyle and healthcare is crossed and when legal action is required. That is very difficult, as we saw recently when the business model of Theranos, the worldwide largest provider of DTC testing, turned out to be a complete fraud. Scientists and physicians alike had relied on Theranos methods. It was claimed that there is a conflict of interest, because they themselves provide diagnostic services and there were attempts to force them to cease and desist from using the Theranos methods.

'It is also highly problematic when physicians use results from lifestyle DTC tests since this basically means that lifestyle test results are jazzed up to be healthcare diagnostic results – but these lifestyle tests follow no legal and technical standards whatsoever. If the patient suffers damages, the physician who accepted the DTC results is liable even though he probably was not involved in the generation of the results at all.'

Do these tests impact on work in the lab?

'One important danger I see is the careless handling of medical data in DTC testing. There is high potential for abuse, particularly with molecular exams. It defeats me how people can thoughtlessly allow 23andMe, a genetic testing company with close links to Google, the use of their genetic and other highly sensitive data.

'Another problem is the waste of healthcare resources through DTC testing: The business model of DTC testing often entails the fabrication of conspicuous findings in order to sell, for example, dietary supplements, or expensive monitoring services. Thus lifestyle tests often lead to complex diagnostic procedures of a perfectly healthy person – with the general public footing the bill.

'A third issue is the media hype surrounding DTC testing, something we have never seen in evidence-based medicine: DTC testing services are regularly promoted in blogs, user groups and the social media. The promotional texts, even though they might be labelled as "advertisement" somewhere, convey images of a certain lifestyle and make claims regarding DTC testing that are in no way supported by evidence. However, we find it impossible to counter these internet trolls with reasoned arguments.'

Should DTC be more strongly regulated?

'The definitions of DTC testing are indeed very complicated and we do see efforts of DTC testing providers to circumvent the healthcare rules and regulations that are in place and necessary to ensure patient safety. Think of the over-the-counter sale of lab tests in pharmacies, or the call for tenders for genetic testing under section 140a of the German Social Code, book V regarding special services.

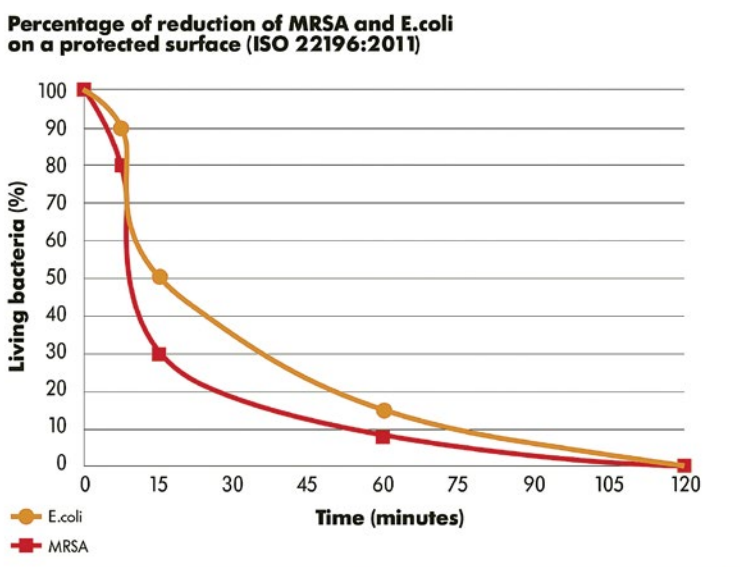
'Moreover, internet offerings and mail order pharmacies cross national boundaries and thus turn many reasonable regulations into blunt instruments. In addition, DTC testing providers legitimise their services by referring to the EU consumer rights directive 2011/83/EU, which is meant to promote free movement of goods and services.

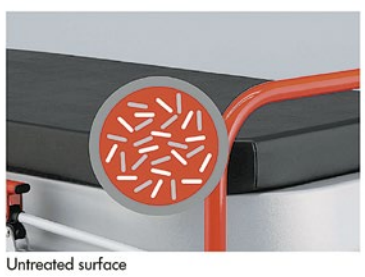
'In my opinion that is dangerous and very naïve: Today, even small forensic DNA specimens provide information on features as such ethnic background, size, hair colour, etc. It is naïve to assume that complete genome sequencing in a lifestyle test done for genealogical purposes does not provide medical data that need to be protected. Consumer protection in DTC testing is marginal. The limitations of the methods are hidden in the small

On offer to the public: testing for a fee

New and improved equipment strengthens hospital hygiene

Coatings defeat patho




Untreated surface


Treated surface

Nosocomial infections are dangerous – sometimes having grave consequences. The German company Schmitz u. Söhn points out that manufacturers of medical equipment and furniture are challenged to keep germs under control and it increasingly focuses on the hygienic aspects of new and further product developments in its closed design of operating tables and antimicrobial coatings.

The firm uses such coatings on all frequently touched surfaces, including side guards and push bars of its stretchers. These coatings are based on innovative silver ion technology that effectively and permanently fights mildew, fungi and even resistant strains of bacteria. Studies show that 80 percent of harmful bacteria on the coating can be removed in just 15 minutes and even 99 percent of germs are eliminated after two hours, the company reports.

Pads attached by adhesive gel

Removable pads are generally attached to couches and transport vehicles using Velcro fasteners, which, due to their uneven structure, are extremely difficult to clean. Schmitz u. Söhne use an adhesive gel to attach pads. This is resistant to disinfectants, features an even surface and makes it possible to thoroughly clean the underside of the pad, the firm adds.

Design and construction of OR tables

The design and construction of the company's OR tables and attachments also have smooth surfaces and a closed design to ensure maximum ease of cleaning. Even critical areas, such as screw heads, are closed or completely covered and, the firm reports, there are virtually no nooks or crannies in which bacteria can multiply undisturbed.

New cleaning shuttle

'A prime example of a new product exclusively developed for hygiene is the Schmitz u. Söhne cleaning shuttle, which for the first time cleans operating tables easily and thoroughly from the bottom,' the firm adds. 'The shuttle consists of a separate, movable frame into which the operating table is placed at maximum height. The supports of the shuttle are positioned directly under the seat section of the table. Afterwards, the staff lowers the operating table again. The chassis lifts off the floor, allowing for thorough cleaning of the underside of the table as well.

Hygiene constantly challenges manufacturers

'We consider hygiene in hospitals to be one of the most pressing current

Professor Matthias Orth MD gained his doctorate in 1994 at Albert Ludwig University, Freiburg, Germany. Following specialist courses in clinical chemistry, internal medicine, microbiology and immunology, he worked at the Institute of Clinical Chemistry and Pathobiochemistry at Freie Universität Berlin. From 2000 to 2003 he was Managing Senior Physician at the Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics at University Hospital Leipzig, gaining his habilitation in 2004. He then became Medical Director of the Institute of Laboratory Medicine at Marienhospital Stuttgart. Orth is a Board Member of the German Society for Clinical Chemistry and Laboratory Medicine, Chairman of the Laboratory Management Section at DGKL and a Board Member of the German Professional Association of Laboratory Medicine.

print and difficult to understand.

'We do need the active support of all lab specialists in order to contain this uncontrolled growth.

Is Europe's situation different in the USA?

'While the overall objective, to protect lab diagnostics, is similar across countries, the legal frameworks differ considerably. In Europe genetic data enjoy particular protection whereas in the USA's lifestyle tests are not per se prohibited. Moreover the rules to ensure quality standards in the labs differ widely. In Germany, for example, quality assurance is concerned primarily with structural quality; in the US it focuses on the quality of the results.

'It's crucial that every country views assurance of patient safety as the interplay of different rules and regulations. We must not undermine very successful quality assurance and patient safety structures by pointing to isolated rules in other countries.'

Emergency POCT

Point-of-care testing can play an influential role in reducing overcrowding in hospital emergency departments, Mark Nicholls observes

Emergency medicine consultant Ulf Martin Schilling MD, based in Linköping, Sweden, believes that the strategic use of point of-care tests (POCT) can improve patient flow through departments and in some cases initially avoid the need for patients to attend.

In a recent symposium, Dr Schilling posed the question: 'POCT in the Overcrowded Emergency Department - Can It Make a Difference?' during the American Association for Clinical Chemistry (AACC) conference, which was held in Denmark in September this year. The use of point-of-care tests in various patient care settings was examined, with a focus on clinical decision-making and improved patient outcomes.

Speaking with European Hospital after the event, he said that, although emergency departments (ED) with increasing public demand are becoming ever more overcrowded, on the spot tests can be used to help alleviate this.

Improvements in the survival rate of critically ill patients in the ED are directly related to the advancement of early recognition and treatment though frequent episodes of overcrowding.

With prolonged waiting times forcing EDs to operate beyond their capacity and threaten to impact upon patient care, he suggested point of care testing can be brought into play at every stage. 'We have good evidence, for example that, if you empower GPs with POCT analysis, the number of unnecessary referrals can be reduced because GPs can reliably rule out disease and do not need to refer some patients,' he explained. 'And if you

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use POCT in the ambulance, you can improve the overall process for the patients because you are winning time within the emergency department.'

Once in the emergency department, POCT can be used at the triage stage to safely identify urgent cases, and save more time as well in the diagnostic and treatment stages. As a result, the process towards one of the main goals of the emergency department will be speeded-up: the decision on whether a patient is admitted, discharged or referred elsewhere.

'At every different step of the emergency process and on every single patient's process you can be losing time,' Schilling emphasised. 'If this happens for a team caring for 6-8 patients, all the different delays in the patient process will accumulate to a critical level. As a result, your team will not be as effective and you find your department in an over-crowding situation.

'Overcrowding is not so much about how much space or how many beds you have but mostly about when emergency department staff cannot work efficiently any more in processing patients. But, if you reduce the delays at the front end, you will have faster processes and you gain time on each patient. Even small earnings in time will give the emergency team the possibility to work efficiently. The key is to have a more efficient process that will reduce the effect of overcrowding and this can be achieved with point of care testing.

'In recent years, particularly during the last decade, POCT has evolved due to new technology, and the range and accuracy of many tests has become better as well as the quality.'

POCT in the ED can include virtually all relevant testing in emergencies, urgent and acute care, he said.

'To be approved by the authorities, POCTs have to follow the same regulations as the core laboratories, which means the major producers must maintain very high standards of quality,' he added.

Dr Ulf Martin Schilling is head of the clinical education and simulation department Clinicum East Sweden and the unit of testing, innovation and technology assessment. A consultant in emergency medicine and specialist in Internal medicine, he is also a consultant in simulation and implementation at the University hospital of Linköping, Linköping, Sweden. His research interests include patient flow, POCT, the economics of the emergency department, and point-of-care ultrasound.

However, in the use of on the spot tests in emergency departments there is inconsistency across Europe in the use of such testing in emergency departments, often due to factors such as the remuneration system, a limited analysis of front-end investment towards cost-return in the overall process, and the policy of the local hospital and trust. To profit from the potential of point of care testing at the pre-hospital, hospital and post-hospital level, Schilling suggests, a knowledge-based change of culture among local staff and management is essential. Training and knowledge about the possibilities – and limitations – of POCT is crucial for efficient implementation of new systems and tests. 'If you can process patients in a much smoother way, it improves flow and reduces the crowding problem.

'Point of care testing,' Ulf Schilling concluded, 'can make a difference in the overcrowded emergency department and can contribute to alleviating the effects of overcrowding.'

ogens

Gel adhesive pads

and future problems in medicine,' says Friedrich Schmitz, managing partner at Schmitz u. Söhne. 'That's why we are doing everything conceivable to control hospital germs and the infections that accompany them. It starts with small details in the design, such as screw covers, and ends with the development of completely new hygiene-oriented products, such as the cleaning shuttle. We will continue to work tirelessly on this issue.'

Changes to intravascular catheter systems in 2017

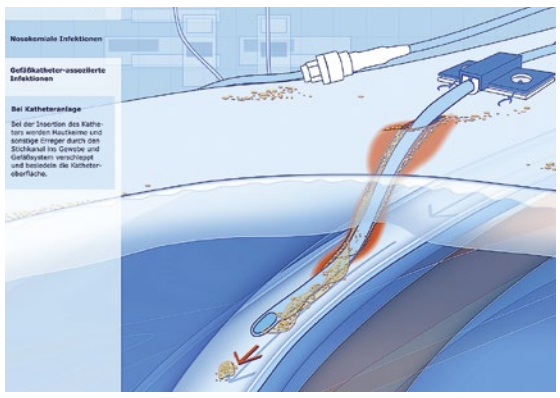
Ousting out-dated recommendations

Report: Brigitte Dinkloh

Recommendations on the currently valid prevention of intravascular catheter-related infections from the Commission for Hospital Hygiene and Infection Prevention at the Robert Koch-Institute (KRINKO) are now 14 years old and therefore out-dated. Much has happened since their first publication in 2002, making an update essential to include the latest developments in medical sciences. We interviewed Dr Christine Geffers, Consultant at the Institute for Hygiene and Environmental Medicine at the Charité Berlin and co-author of a new recommendation to be issued in the New Year.

'This recommendation was overdue for a revision, and such an important guideline should, in fact, be updated in much shorter intervals of five to six years,' Geffers points out. 'This cannot always be assured due to the large number of recommendations that need to be issued,' Geffers, who is a colleague of Professor Petra Gastmeier at the National Reference Centre for the Surveillance of Nosocomial Infections, first mentioned data sources. Recommendations currently in place are based on 219 sources; the new recommendations quote more than 600 sources. 'What was assumed or believed back in 2002 can now be safely confirmed by the number of studies carried out since.'

Not only the quantity but also the quality of the underlying data has improved. 'Studies carried out prior to 2000 are now considered out-dated,' Geffers confirmed. 'These days, the expectations of quality with regards to ethics, for instance, are very different to what they were 15 years ago, when everyone had the freedom to carry out studies based on their own ideas. Therefore, the objective now is to draw on more recent studies that comply with current quality standards.'



To prevent intravascular catheter-related infections further, the new recommendations cover non-tunnelled central venous catheters (CVC), peripheral venous catheters and arterial catheters

The new recommendations cover non-tunnelled central venous catheters (CVC), peripheral venous catheters and arterial catheters. Port systems, partially implanted intravascular catheters and intravascular catheters for newborns are no longer covered, with the latter now being covered by a separate KRINKO recommendation. There is also a lack of recommendations on how to deal with large bore vascular access required for extracorporeal oxygenation or decarboxylation (the artificial lung), because there are hardly any studies available on this topic.

As it is not possible to introduce all innovations here, Geffers lists some examples. The preferred access point for a CVC in the subclavian vein is no longer recommended, with no recommendation being made either for or against this access. 'The only recommendation here is not to use the jugular vein for patients with a tracheostomy who need a CVC. It would be too complex to list all the changes in detail,' says the specialist for Infection Prevention and Control and Environmental Medicine.

Another new recommendation is that peripherally inserted CVCs should no longer be preferred. Regular, daily monitoring and documentation of the diagnosis during ward rounds is another significant change. Going forward, doctors will have to monitor on a daily basis whether the CVC should remain in place or not. There is also a change regarding access to the system. The new recommendation stipulates that the connections, such as the three-way tap, must be disinfected after every use.

However, there is no change to the recommended time in situ for the catheter. 'The objective is still to remove it as soon as possible, which is also why daily monitoring is advised, to see if the indication for leaving the catheter in place is still valid,' Geffers explains. 'There were no maximum time limits for leaving CVCs in situ in the 2002 recommendations, and there won't be any in the 2017 recommendations, either. The current recommendations advise against changing catheters regularly, and this will continue to apply. The infusion tubes were supposed to be changed every three days, but the new recommendations advise at least four day intervals between changes.'

A large part of the recommendations revolves around staff training. This should ideally be carried out in small groups and should include a lot of practical exercise. In future, important preventative measures are to be focused on with the help of specific campaigns. The fitting of peripheral cannulas was discussed in the context of using specialist catheter teams – as seen in the US – but the new recommendations stipulate that it is preferable to ensure that all team members are capable of changing catheters, and to check that this is the case. 'The new recommendation aims to minimise the risk of infections further still. However, regardless of the numerous new recommendations, up till now, not everything that has been practiced on the wards has, in fact, been wrong,' she concedes.

The recommendation will certainly contribute towards increased patient safety. The prevention of nosocomial infections by the management of medical institutions as required by paragraph 23(3) of the Law on Infection Prevention and Control is usually ensured through the implementation of the KRINKO recommendations. 'As these are supposed to reflect the latest findings of medical sciences many medical institutions adhere to them,' Geffers points out. 'The recommendations are therefore essentially binding, particularly when litigation is concerned. In these cases it is important to prove that the recommendations were implemented, or to substantiate why they were not adhered to.'

In 1996, **Dr Christine Geffers** began her career as a research assistant at the Institute for Hygiene and Environmental Medicine, then part of the Free University Berlin and now part of the Charité University Medicine Berlin. After qualifying as a specialist for Hygiene and Environmental Medicine she became a consultant at the Institute for Hygiene at the Charité in 2001. In 2003/2004 a grant from the Walter Marget Foundation for the Advancement of the Study of Infectious Diseases facilitated a research stay with Professor Barry Farr at the University of Virginia, USA. In 2015, Geffers wrote her habilitation in Infection Prevention and Control. Her focus is on the surveillance of nosocomial infections, nosocomial infections in newborns and the prevention of catheter-related sepsis.

The Heraeus Lunch Symposium

Painful knee prosthesis: loose, infected or both?

Report: Beate Wagner

The implantation of knee and hip joints is considered one of the success stories of recent years. But periprosthetic joint infections (PJI) are one of the severe complications, with an infection rate of 2%. The probability of revision surgery increases with concomitant diseases such as rheumatoid arthritis, with fracture prosthesis or after previous surgery.

The challenges in diagnosis include low-grade infections, small colony variants, contamination of samples, mixed-species colonisation and increasing development of resistance: Apart from MRSA the other problematic pathogens include gram-negative bacteria (MRGN) and vancomycin-resistant enterococci (VRE).

Treatment is impacted by old age and multimorbidity. 'Often, high concentrated antibiotics cannot be administered,' says Professor Georg Matziolis MD, Senior Consultant at the Clinic for Orthopaedics and Emergency Surgery at the Eisenberg Waldkrankenhaus. 'Topical treatment with antibiotics is becoming increasingly important.'

'Firstly, it is important to establish whether a PPI or aseptic loosening is present,' explains Professor Johannes Holinka MD, from the Medical University of Vienna. In 25% of cases a PJI is the reason for revision and, in 16%, it's mechanical loosening.' The anamnesis, followed by radiological and clinical examination along with laboratory diagnosis of blood, synovial fluid, tissue and histology provide the indications required.

From left: Ákos Zahár, Assistant Professor Johannes Holinka and Professor Georg Matziolis

Microbial detection as the primary objective of the diagnosis of low-grade infections often proves difficult. 'In up to 30% of cases no micro-organism can be cultivated,' Holinka points out. The specificity of microbiological cultures increases with the number of samples. 'Three to six intraoperative samples are ideal, and in cases of low virulence organisms or after previous administration of antibiotics we require up to ten.'

Sonification is more significant than a tissue culture. As a biomarker, Alpha-defensin facilitates the detection of a PJI because it is not impacted by antibiotics. Quantitative measurements have shown a sensitivity and specificity of 96% and 97% respectively. The procedure only has one disadvantage: 'Although the diagnosis is as good as certain it does not provide microbial detection,' Holinka says. On the other hand, Multiplex-PCR (mPCR) of synovial fluid with Unyvero ITI for instance is often decisive for treatment.

'The analysis can be carried out with minimal effort and with no need for specialist staff trained in molecular biology or a special infrastructure,' he adds. 'Microbial detection including resistance markers is available after five hours, even for low virulence organisms that normally take 14 days to cultivate.' Combined with the culture grown, the sensitivity is around 90%.

Treatment of a PJI is carried out via one- or two-stage revision and high-dose antibiotics. With an eradication rate of 89.2% and 90.6% respectively the effectiveness of both procedures is very close. 'Successful one-stage exchange requires microbial confirmation, radical debridement and effective antibiosis with systemically and locally applied antibiotics,' says Dr Akos Zahar, orthopaedic specialist at the Helios Endo-Klinik, in Hamburg. The key to success for the one-stage procedure lies in the close multidisciplinary cooperation between surgery, microbiology and infectiology. 'For one-stage exchange the use of industrially manufactured, antibiotic-loaded bone cement (such as Copal G+C or Copal G+V) is recommended to achieve the high concentrations required for local antibiotics therapy without actually having to add antibiotics yourself. 'This avoids turning the doctor into a manufacturer of medical products,' the expert underlines. With cemented one-stage exchange, antibiotical treatment can be cut from several weeks to 14 days.

Two-stage exchange is the gold standard worldwide. This is indicated in cases of negative bacterial culture, difficult-to-treat pathogens as well as in the case of soft tissue defects that require a step-by-step approach. Antibiotic-loaded bone cement is used as a spacer during the prosthetic-free interval and for the re-implantation during the second operation.

'Dynamic spacers (such as those made from Copal knee moulds) are more effective than static ones,' Zahar points out.

'They offer more patient comfort, are easier to re-implant and the functionality is better,' adds Matziolis.

The abrasion of cement and ceramics particles appears clinically irrelevant. There is currently little evidence available for mobile spacers compared to static spacers. However, the advantages of mobile spacers for dead space management and local antibiotics treatment prevail. Two meta-analyses show that the range of motion (ROM) for a mobile spacer is better by +8 degrees, and superior in lowering re-infection rates, reducing bone loss and easing re-implantation.

Matziolis talked about the superiority of spacers made from industrially manufactured, antibiotic-loaded bone cement compared to alterna-

Call to re-evaluate sepsis screening tool

Expert declares updated criteria for sepsis identification is not early enough. Mélisande Rouger reports

New criteria used as an initial screening tool in the emergency department need to be re-evaluated, a specialised surgeon will highlight in a dedicated talk during the Spanish national congress of surgery this November.

In Spain sepsis affects 50,000 people and is responsible for 17,000 deaths each year (The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb 23;315(8):801-10).

Early detection of infection, before patients must be admitted to intensive care, is essential to trigger appropriate treatment and improve outcome.

A commonly used strategy among doctors to identify a suspected infection and evaluate severity has been to use criteria defined by experts. The Systemic inflammatory response syndrome (SIRS) criteria, which rely on the degree of hypoperfusion and inflammatory response to determine the presence and degree of the infection, have long served as a reference in clinical practice and research. However, many practitioners have insisted the SIRS are not sensitive and specific enough. In fact, the controversy over these old criteria pushed the international consensus responsible for setting sepsis criteria to issue new measures earlier this year.

These experts updated the definitions by putting the focus on low blood pressure, high respiratory rate and altered mentation as means to recognise sepsis and septic shock for patients inside and outside the ICU.

Dr. Ines Rubio-Perez with the team from La Paz Hospital in Madrid

The new criteria have been named the qSOFA (Quick SOFA Score), and many thought they would help gain time in patient management.

However, the authors of a more recent study have concluded that the qSOFA does not help to evaluate patients in the Emergency Department who are not yet in need of critical care (qSOFA, SIRS, and Early Warning Scores for Detecting Clinical Deterioration in Infected Patients Outside the ICU. Churpek, Snyder, Han, Sokol, Pettit, Howell, Edelson).

Thus things are back to square one and there hasn't been much progress in speeding the identification of effective criteria for early diagnosis, Dr Ines Rubio-Perez from La Paz Hospital in Madrid, explained. 'The change of parameters was meant to improve everything. But, according to the new study, the qSOFA are not that good in diagnosing patients on time; actually if you have to monitor altered mentation it means it's a little late already,' she said. 'qSOFA detect mortality very well but they are not early criteria. So there's not much difference between the old and the new, and many people are discussing the utility of these criteria in the emergency setting.'

Rubio-Perez, a colorectal surgeon with special interest in surgical infections, will join a symposium on intra abdominal infection diagnosis and treatment update during the meeting. In her opinion the absence of a gold standard in sepsis management is due to the complexity of the disease. 'What happened again with the Sepsis 3 consensus is that things don't work as well in practice as in theory. Sepsis is a complex process and it's complicated to define uniform standards. We still need to revise our criteria, or make a combination between the SIRS, the qSOFA or other scores.'

To speed things up, Madrid hospitals started the Code Sepsis initiative, similar to Code Stroke, and in which healthcare members are put on alert in case of suspected sepsis to trigger the appropriate chain of action.

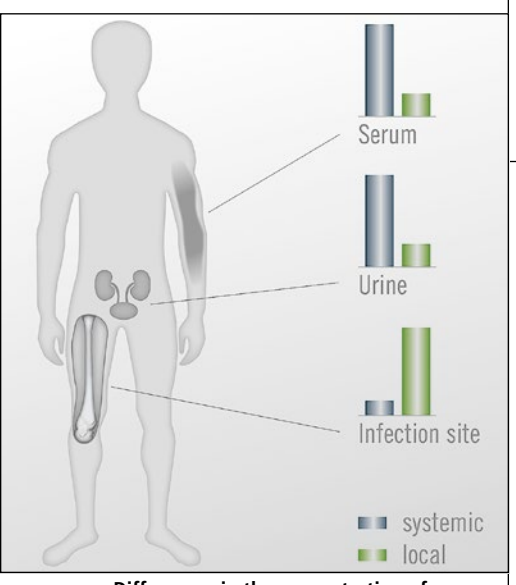
'Initiatives like the Surviving Sepsis campaign and Code Sepsis can offer simple pathways and identification systems to diagnose patients with sepsis early. This must be an institutional and multidisciplinary effort. A few other regions in Spain have done the same with successful results,' Rubio-Perez pointed out. Sepsis is a common scenario in abdominal emergencies, for instance in peritonitis or appendicitis, and treatment relies on antibiotic and surgical therapy.

Besides finding the appropriate diagnostic criteria, the other challenge in sepsis management is antibiotic resistance. 'A patient presenting with an infection due to multi-resistant bacteria may not respond to usual treatment, as the initial antibiotic may not cover appropriately. This significantly increases morbimortality.'

Rubio-Perez, PhD was on the topic, suggests looking at risk factors, such as previous antibiotic intake, or recent hospitalisation, prolonged stay in long-term care, or residential home, a daily hospital visit for dialysis, and other clinical factors, including diabetes, immune suppression, repeated urinary tract infection, etc. 'Having suffered a previous super resistant bacterial infection, i.e. being a carrier, augments risk for a patient to present with a clinical infection,' she added.

Complications increase in post-surgery patients who develop a nosocomial infection. Treatment may be only one or two antibiotics, because of resistance, and this may also substantially augment morbidity.

After completing her residency in general surgery in 2012 at Princesa Hospital in Madrid, **Ines Rubio-Perez MD** became a staff surgeon in the colorectal surgery unit at La Paz University Hospital. Her research activities include the study of clinical profiles and risk factors of multi-resistant infections in surgical patients – the subject of her PhD thesis in 2015. She is a member of the board of the Surgical Infections Section in the Spanish Surgical Association (AEC), and Councillor and Educational Committee member of the Surgical Infection Society - Europe (SIS-E), where she strives to involve surgeons in the knowledge and importance of infections.



Differences in the concentration of antibiotics with local and systemic antibiotics administration

tives with antibiotics added manually. The release rate of the antibiotics gentamicin and clindamycin from a spacer made with industrially manufactured bone cement (Copal G+C) is higher at all points in time.

The team around Mike Reed at Northumbria Health Care (UK) confirmed a reduction of infections with the use of antibiotic-loaded cement in the prosthetic care of femoral neck fractures in a randomised examination. The study proves that dosage and release are decisive. Standard cement (Palacos R+G) was compared to high dose dual antibiotic cement (Copal G+C).

The reduction in the infection rate for deep-lying infections was 3.5% with Palacos R+G; for Copal G+C it was only 1.1%.

Assessing the performance of emergency departments

Many units themselves need emergency care

Germany's hospital emergency departments run up a loss of more than one billion euros every year. EH correspondent Ralf Mateblowski asked Dr Thomas Fleischmann, Medical Director of the Department of Interdisciplinary Emergency Medicine at Westküstenkliniken in Schleswig-Holstein, about the fragile state of the emergency department.

According to Thomas Fleischmann, specialist in the reorganisation of emergency departments, care for emergency patients rakes up a loss of about one billion euros every year.

Comparing apples and oranges

'The loss generated in emergency departments is primarily caused by a significant increase in out-patients – who today account for two thirds of all patients presenting to the emergency room. The major problem is the reimbursement system via the German physicians' associations, the Kassenärztliche Vereinigung. To be more precise: physicians in the emergency room are reimbursed exactly like office-based physicians. However, the emergency room is open 24/7, 365 days a year, whilst a doctor's office is open 30 hours a week.'

A second difference, Fleischmann points out, 'Are the provision costs of an emergency department, be it for physicians or nurses, for CT, cardiac cath lab or intensive care. The moment you subtract these provision costs from the total costs and add comparable costs for 24/7 care to the profit and loss account of a doctor's office the difference between hospital emergency room and doctor's office is not that big any more. Currently, costs in very different infrastructures are reimbursed identically – but whilst this reimbursement might be sufficient for a doctor's office it will never even come close to covering the additional staff and operating costs a hospital's emergency room incurs with its around-the-clock service.'

Dedicated to improve emergency flow, Thomas Fleischmann says: 'Modifications to the hospital structure law are insufficient, but are a clear step in the right direction.'

Internal considerations

'When we look at internal factors, our emergency departments don't look too bad. Overall, we provide good healthcare. However, there is room for improvement. Unlike other industrialised countries, in Germany it's mostly the junior physicians rather than specialists who staff the emergency room.'

Specialists are in short supply

'Germany is one of the few countries – not just in Europe, but also among high-income countries worldwide – that does not provide regulated training for emergency room staff. The result is that inexperienced junior physicians, trying not to make mistakes in the emergency room, tend to do too many exams of patients with low-degree conditions and to admit too many people as in-patients. This issue can only be solved with adequate and defined training in clinical emergency medicine.'

Going forward

'Most importantly, emergency care must be financed; we must not allow it to starve to death. Secondly, the quality of care has to be raised to specialist physician level for each patient to receive exactly the type and level of care he or she needs – not more, not less.

'Let's look at the triage categories: red, orange and yellow – these are patients with medium to severe conditions. Green and blue are patients with minor problems and injuries. Patients with medium to severe conditions account for about 60 percent of cases; the remaining 40 percent are greens and blues. It's the latter category that is rapidly increasing. In my opinion, care for patients in the triage categories red and orange is very good, but we do offer too much medicine to the others.'

Light at the end of the tunnel

'The problem of under-financed emergency rooms is not a German problem, but a problem that's present in many high-income countries, such as the USA. In Germany we cannot – and must not – wait for an international solution; we must find our own direction. To be fair, we are witnessing a historic change: The coalition contract between the German government two parties mentions emergency departments – for the first time ever! Emergency care is recognised as one of the four pillars in the hospital structure law. That is new. While modifications to the hospital structure law are not sufficient, they are a clear step in the right direction. They show that German politicians have recognised the problem.'

Conclusion

'Beyond the fundamental and politically necessary changes, there are no simple solutions for the individual emergency room. Optimisation of emergency care will not result from one single measure but rather from the result of the package of measures to increase efficiency, lower costs and improve financing. Germany has to overcome two major challenges: The extreme shortage of emergency professionals – both in the medical and in the nursing sector – must be addressed. And secondly, no matter how we look at it, we must not allow emergency care to be atrophied for business reasons.'

Thomas Fleischmann, MD was among the first German physicians to pass the European Board Examination in Emergency Medicine (EBEEM) and, in 2014, he completed his Master of Health Business Administration (MHBA) course – top of the year's class.
Having formerly successfully reorganised emergency departments in Salzgitter, Frankfurt-Höchst, Sanderbusch and Hirslanden (Zurich, Switzerland), he was appointed Medical Director of the Emergency Medicine Department of Westküstenklinikum Heide, this summer.
A specialist physician for general medicine, emergency medicine and clinical emergency medicine, and Fellow of the Royal College of Emergency Medicine (FRCEM, UK) and of the European Society for Emergency Medicine (FESEM), he has received many awards for his dedicated work.
He has also edited several textbooks on emergency medicine and co-authored the European curriculum for this specialty.

Congress on emergency medicine

The 11th European Congress of Emergency Medicine will be held from 23 to 27 September 2017 in Athens, Greece. Congress president is Dr Roberta Petrino.

For the first time, there will be a new congress format in a move to transform this event into an opportunity for learning and teaching, to integrate the different professionals in emergency medicine – doctors, nurses and trainees.

Further information:
www.eusemcongress.org