

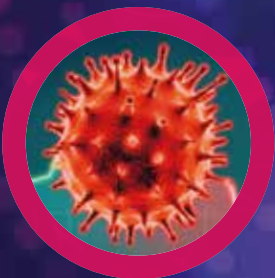
THE JOURNAL FOR SCIENCE, ENGINEERING AND TECHNOLOGY

advances

WALES

T cell test to help scientists understand Covid-19 immunity

A Welsh company is developing a new type of test for Covid-19 which can identify the presence of virus specific T cells in blood.



IN THIS EDITION:

How Welsh expertise has helped in the fight against Covid-19



Llywodraeth Cymru
Welsh Government

Covid-19

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Leading the way on lung ultrasound to manage Covid-19



Advances Wales showcases the latest news, research and developments in Welsh science, engineering and technology. This edition and past editions can all be viewed online.

Advances Wales continues to highlight developments in Welsh science and technology during the Covid-19 pandemic.

This edition of Advances Wales features some examples of new technologies that have been developed and groundbreaking research that has been undertaken across Wales in response to Covid-19.

Welsh innovations for Covid-19 treatment include a ventilator designed to address shortages by being cheap and quick to assemble (page 6), as well as a low-cost, made-in-Wales blood oxygen monitor (page 16).

Meanwhile, scientists based in Wales are working to develop a technology that can quickly decontaminate ambulances (page 11) and to create a new generation of biocidal face masks (page 19). Also in the field of infection control, researchers at a Welsh university are monitoring sewage around the UK to see if it can provide an insight into Covid-19 rates in different areas (page 8).

In this edition, you'll also find the stories behind several different Covid-19 tests that are currently in development in Wales, including one that has been adapted from a new UTI test (page 7) and another that focuses on T cells and could prove particularly useful in vaccine development (page 14). Additionally we look at how a Welsh company is working to enhance an existing test by making it digitally connected (page 17).

This edition of Advances Wales can be viewed online, as well as past editions.

Sophie Davies
Editor

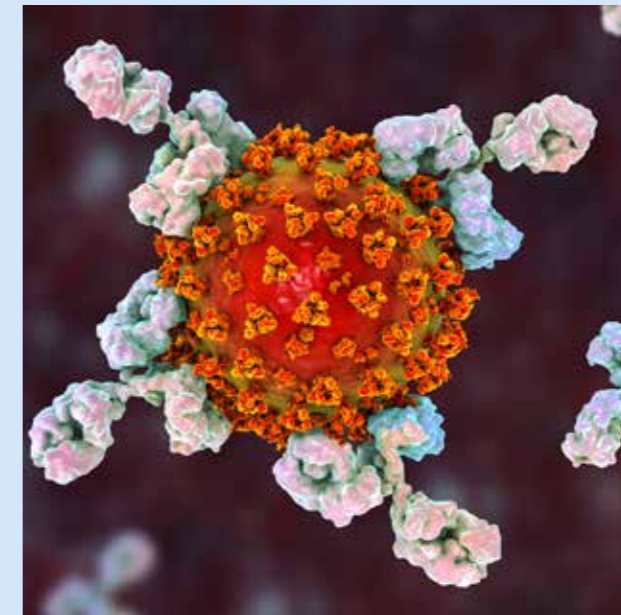
Wales-based manufacturer to produce Covid-19 antibody tests

Production of Covid-19 antibody tests is underway at Ortho Clinical Diagnostics' manufacturing facility in Pencoed.

Working in partnership with Public Health Wales, Ortho will provide Covid-19 assays to support testing across Wales. The tests detect antibodies that can be used to identify an immune response confirming a previous and recent Covid-19 infection, and may be critical in back-to-work strategies.


The company has secured FDA and CE certification for its antibody tests, which offer 100 per cent specificity to help reduce false positives, ensuring that people will not be identified as having an immune response to the virus when they do not.

Paul Hales, Senior Director of Operations at Ortho, said: "We have built a deep manufacturing expertise here in Wales over many years enabling us to produce these important products. The team has been working day and night to reach a mass scale of production of our Covid-19 assays. We believe every test is a life and are proud to see these kits being used in Wales."



"Antibody testing is an important part of our strategy to counter the spread of Covid-19 and to help us understand who has had the disease. Knowing that the production of the test will be local to us in Wales was of great importance to us as we determined which suppliers to rely on."

David Heyburn,
Head of Operations for
Microbiology and Health
Protection,
Public Health Wales

 www.orthoclinicaldiagnostics.com

Innovation grant awarded to face mask comms aid



Technology Design and Dr Arif Reza Anwary, an innovation technologist at Swansea University Medical School. MaskComms is now set to go into production in North Wales.

"Communication is essential during procedures where the anaesthetic and surgical teams work closely but health and safety is also paramount, so their FFP3 masks cannot be removed to talk to each other. The downside to wearing facial masks is that our voices become muffled and indistinct, and we cannot read facial cues. I proposed a solution which allows a device to be placed in any mask, which can transmit to every colleague, or to one communal speaker without compromising the PPE."

Dr Simon Burnell,
Consultant Anaesthetist

A communication aid for frontline health staff wearing face masks has won first place and an £8,000 grant from the Welsh Health Hack.

MaskComms is a microphone designed to fit inside a face mask and transmit voice through wireless to a wearable loudspeaker. It was developed in

response to the NHS identifying that the wider use of facial masks in hospitals has reduced the ability to communicate effectively.

The project is led by Dr Simon Burnell, a consultant anaesthetist at Betsi Cadwaladr University Health Board, in collaboration with Wyn Griffith Designs, product designer Thomas Turner of Ember

 www.swansea.ac.uk

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Advances raises the profile of the technologies and expertise available from Wales in order to facilitate collaborative relationships between organisations and individuals interested in new technologies and innovation.

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Drug discovery platform for Covid-19 on the horizon

Moleculomics has been awarded funding for technology development to find drug treatments for Covid-19 and other viral threats.

The new platform, GRASP (Generic Rapid Antiviral Screening Platform), will seek to get ahead of emerging strains of the virus by simulating the effects of mutations before they happen, and screening the new protein targets against libraries of drug compounds.

"The SARS-CoV-2 virus is mutating, though not particularly rapidly. There are several strains in circulation around the globe and the virus is still undergoing about 25 mutations per year. It is likely in time that these mutations will affect viral structure, drug specificity and pathogenicity, opening up new opportunities for drug targeting with regards to the current pandemic and future viral threats."

Dr Jonathan Mullins
CEO, Moleculomics



The Swansea-based company recently developed the Human3DProteome platform, which contains the 3D structures of all of the proteins (receptors, transporters, enzymes, etc) in the human body, and the Hit2 Lead Portal, which provides a one-stop-shop for protein modelling and drug screening at all scales. GRASP will be the first dedicated antiviral screening platform to be developed by the company.

The team will be working in close collaboration with academic and industrial partners, and the screening results relevant to treatment of Covid-19 disease, featuring interactions with approved drugs and wider chemical space, will be openly shared with partners and on the project website from September.

 www.moleculomics.com

Antibody test reaches development milestone



A lateral flow antibody test for Covid-19 developed by the UK-Rapid Test Consortium (UK-RTC), including Crumlin-based BBI Solutions, has reached a major milestone in its development.

The UK-RTC has announced that its test has reached the 'design freeze' stage. This means that the test has met the required performance characteristics, and the production specifications of the assay have now been

set. The next stage will see the scale-up of processes in readiness for manufacture.

Tests carried out prior to reaching the design freeze stage reported a 98.6 per cent accuracy. The consortium is continuing to work with the regulatory authorities to ensure approval of the test as quickly as possible.

As part of the team, Crumlin-based BBI Solutions is optimising its smartphone based reader technology for this application. The company's technology will guide users at home through performing a test, before

"BBI have been at the forefront of using mobile technology to support point of care testing and the transformation that new technologies bring to this market. We are delighted to be part of the solution; from developing key components of the test to supporting manufacturing capacity and providing this pivotal mobile technology that will enable diagnostics to be delivered on a scale the UK has never seen before."

Dr Mario Gualano
Chief Executive, BBI Group

securely sharing the results directly with the NHS. The process will help ensure that people who have never performed a test like this before will get the right result and feel confident in understanding it, while making sure that the NHS receives all of the data from each test to help them plan and manage the disease's progression.

 www.bbisolutions.com

IN BRIEF

Wales plays key role in urgent research

Wales is playing a key role in the UK-wide effort to find treatments for Covid-19 patients through research. Multiple urgent public health research studies, set up through Health and Care Research Wales, are underway across the country. One such study is the Randomised Evaluation of COVID Therapy (RECOVERY) trial, testing to see if existing or new drugs can help patients who have been admitted to hospital with confirmed Covid-19. It is the world's largest randomised clinical trial of potential Covid-19 treatments, led by the University of Oxford and funded by the Medical Research Council. Health boards in Wales are also taking part in REMAP-CAP, a platform trial for severely ill patients with Covid-19. This trial, led in the UK by Imperial College London and funded by the University Medical Centre Utrecht, is testing multiple treatments at the same time, for patients admitted to intensive care with severe community acquired pneumonia.

Unmanned aerial system in development

Aisymmetrix, the Welsh subsidiary of Manna, has received funding to develop an unmanned aerial system with multiple novel features to enhance flight safety. Their aim is to revolutionise last-mile logistics through the use of advanced unmanned aircrafts. The initial target market is the food delivery industry, where they anticipate manufacturing unmanned aerial vehicles to carry prepared food directly from restaurants and kitchens to consumers' houses. Manna wants to provide a total solution for the ordering and delivery infrastructure for food retailers. The engineering team at Aisymmetrix is working the system, and the new funding will help with the development and validation of an advanced prototype. In the long term, the project will contribute to the growth of the company, with the potential to create innovative products and jobs within Wales.

Funding for digital tech in response to Covid-19

Five digital health initiatives have been awarded funding as part of a £150,000 call for new and innovative ways to use digital technology in response to coronavirus and beyond. The call to action was coordinated by Digital Health Ecosystem Wales, a collaboration between Life Sciences Hub Wales and the NHS Wales Informatics Service (NWIS). The five winners were: PhysioNow by Connect Health, a physiotherapy chat-bot providing 24/7 triage and support for musculoskeletal conditions; Medopad by Huma Therapeutics, a real-time remote patient monitoring system allowing for symptomatic patients to remain home rather than be admitted to hospital; MedTRIM by DNA Definitive, enabling support for those exposed to trauma in the workplace to continue digitally; CliniTouch Vie by Spirit Digital, supporting the management of COVID-19 patients in the community post-discharge with patient monitoring; and SPOT by HealthyIQ, a wound assessment app which scans wounds and shares images for further assessment.

Hydroponics technology secures investment

Phytoponics, which featured in Advances 80, has recently secured £500,000 funding. The company specialises in the design, development and supply of Deep Water Culture systems for large scale sustainable hydroponic crop production. Phytoponics is headquartered in Aberystwyth and was co-founded by Adam Dixon, while he was still a student at Cardiff University, with the aim of delivering optimised hydroponic systems to produce better crop yields than traditional systems. The company now has a number of controlled-environment glasshouses equipped with various configurations of its hydroponics technology growing different varieties of tomatoes, cucumbers, snack peppers and strawberries, in addition to other experimental crops. Edward Baarda Limited has also become the first commercial grower in the UK to deploy the Phytoponics technology at scale, growing tomatoes hydroponically without a rockwool substrate.

Innovation award for Swansea professor

Professor David Worsley has received the prestigious award for Innovation, Science and Technology at the St David Awards 2020, which recognise exceptional achievements by Welsh citizens. At Swansea University, Professor Worsley is a member of SPECIFICS Management Team, a Tata Steel-sponsored Professor and Vice President of Innovation. During his 30-year career at Swansea, Professor Worsley has secured more than £100 million of research funding. He has driven world-leading PV research through projects like SPECIFIC, SUNRISE, ABC, SUSTAIN, SAMI, and the numerous spin-out organisations that exist as a result. He has also built strong partnerships in Wales and beyond – with universities such as Cardiff, Cambridge and Oxford, as well as with industry including NSG Pilkington Glass, Akzo Nobel and many SMEs.

AI firm develops new tools with funding boost

Artificial intelligence specialist Nightingale HQ, based in Caerphilly, has been awarded £50,000 to support businesses across the country, making them better placed to deal with future disruption similar to that of the Covid-19 pandemic. The company's AI Productivity Toolbox project will support SMEs across the UK that need to lower costs by creating six, free-to-use, AI-based tools. The project will include the launch of chatbots, meeting captioning and transcript software, sales AI, cognitive AI-powered invoice processing, social listening AI and productivity-boosting robotic process automation. Steph Locke, data scientist and chief executive of Nightingale HQ, said: "Our mission has always been to help organisations and businesses get AI-ready. So when we spotted the opportunity, we felt that a project to create free and easy-to-integrate AI tools would really help those struggling to keep costs down whilst also growing their enterprises."

Research looks for weaknesses in the virus

A researcher from Aberystwyth University has developed a method of identifying potential hotspots in the coronavirus, which could help develop vaccines and drug treatments. As part of a team from Aberystwyth and Edinburgh Universities, PhD student Nicholas Dimonaco contributed to an international research event, bringing together experts including data scientists, biomedical researchers and health professionals to work on coronavirus research. His team was among four winners out of 1,500 people who applied to take part in the event and 20 teams chosen to make formal presentations. The team compared mutations in the Covid-19 virus in people with similar viruses in bats and other animals such as pangolins. Mr Dimonaco said: "By identifying the variations within, and the similarities between, these genomes, I hope it will enable thousands of laboratories around the world to find potential drug treatments and vaccines. Because of the current health crisis, we are continuing to meet as a team every week at the moment. We are also using existing technologies to speed-up the research process."

Research centre founded for plastic waste

A new research centre has been established at Bangor University to study the growing problem of plastic waste. The Plastic Research Centre of Wales (PRC Wales) is the first of its kind in the country and brings together a wide variety of academics, students, organisations and industries. Projects taking place include: the Centre for Environmental Biotechnology looking at how microbes are attaching themselves to plastics; the Bangor Wetlands Group looking at the presence of microplastics in UK inland waters and National Parks, alongside developing wetland ecosystems to remove plastic particles from our waterways; and the BioComposites Centre investigating alternatives to plastic packaging and most recently working with willow. Scientists are also mapping the movement of microplastics in soils, rivers and coastal waters, looking into the effects plastic has on organisms and habitats and creating uses for waste plastic.

Medtech company joins Covid-19 fight

Benson Viscometers is helping in the fight against coronavirus since its clinical laboratory diagnostic equipment has been shown to have a key use for medical teams treating Covid-19 patients. The Haverfordwest-based company, which featured in Advances 91, designs and manufactures clinical viscometers to test the viscosity of bodily fluids. The plasma viscosity test is an important diagnostic aid for a range of conditions, and has now been identified by scientists as important in monitoring critically ill Covid-19 patients. In these patients, a rise in plasma viscosity is due to an increased concentration of a clotting protein called fibrinogen. This raised level of fibrinogen increases the risk of a blood clot forming and could explain why a large proportion of the deaths from Covid-19 are from thrombotic episodes. As higher plasma viscosity is linked to higher levels of complications, the test could aid early identification of patients who are likely to have more severe symptoms.

Bee app creates buzz

Citizen scientists across the UK are being urged to map bee-friendly plants using a Spot-a-Bee app developed in Wales and Scotland. Created by Cardiff University's School of Pharmacy and Pharmaceutical Sciences and the University of Glasgow, the app invites users to submit photos of plants that attract bees in their garden or local area to help plot a map of plant distribution across the UK. Professor Les Baillie from Cardiff's @Pharmabees project explained: "By downloading and using the app, people can help us better understand the behaviour of honeybees and the plants they need. Spot-a-Bee has grown wings since it began life at Cardiff and we're delighted to be working with Glasgow to engage a new community of nature lovers." It is hoped that the data gathered through the app will be useful for conservation, as it will provide information about plants that bees like and could encourage planting of them to create bee-friendly habitats. It could also help with Professor Baillie's research into the anti-microbial properties of honey.

Collaboration leads to new life-saving ventilator

Experts from Swansea University and University of Wales Trinity Saint David have collaborated to design a new ventilator that can be built quickly from local parts and used for patients with severe coronavirus.

Ventilators are crucial in treating many patients with Covid-19, so as the pandemic continues, global demand for them will remain high. However, a problem with existing designs is that they can be either quick to build or able to treat complex cases, but usually not both.

Designs that are quick to build can only be used to treat patients with mild lung injuries. On the other hand, current models that are suitable for more complex cases need lots of different parts which require specialist tooling. This makes it impossible to build them quickly in large numbers, as medical components are difficult to obtain at the moment due to demand. The new ventilator, called CoronaVent-One, stands out because it has been designed to offer the best of both worlds.

The team behind the new design was made up of doctors, engineers, designers and industry partners. These included Dr John Dingley and Dr Dave Williams, who are consultant anaesthetists in the NHS with teaching roles at Swansea University Medical School, along with Swansea University College of Engineering, Swansea University's Health Technology Centre (HTC) and the University of Wales Trinity Saint David's Assistive Technologies Innovation Centre (ATiC).

The CoronaVent can be manufactured quickly and cheaply in bulk because all the components are generic and can be locally manufactured. It does not rely on extended

international supply chains, enabling Welsh industry to build long term resilience to respond to future health challenges. The device can run from any oxygen source, as opposed to just hospital supplies, and can potentially be built by a wide range of manufacturers.

It also incorporates the sophisticated modes of operation needed to treat patients with severe coronavirus infection, which would normally only be found on more costly



machines. A small computer with a display allows full control of the main parameters for ventilating a Covid-19 patient.

The team are currently seeking regulatory approval for their design and are looking to take the device into mass production.



“Further surges of coronavirus and other pandemic virus infections are expected to occur in coming years, and it is essential that a stockpile of ventilators with suitable functionality is available. There is also a global need for low cost, high specification ventilators in other countries affected by the pandemic.”

Dr John Dingley

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Swansea

Adapting a UTI test to diagnose coronavirus

The University of South Wales is developing a rapid diagnostic test for Covid-19 with help from the Welsh NHS and industry partners.

Researchers adapted a technique that they had been developing for the diagnosis of urinary tract infections, which featured in Advances 92, to create a new test that detects whether people are actively infected with the underlying SARS-CoV-2 virus.

The test is designed to be low-cost and quick. It uses a different method and chemicals to the current accredited tests, thereby avoiding supply bottlenecks for the components.

Since an initial evaluation in collaboration with Cwm Taf Morgannwg University Health Board, the team is now working to optimise their test for use at point of care. The molecular technology, which is based on loop-mediated isothermal amplification of DNA (or LAMP), lends itself to point of care testing because no complex sample processing or expensive equipment is required. The approach involves a novel swabbing and sample extraction technique to reduce cross-contamination and biosafety issues, as well as the time taken to process the results.

The team has been working with Electronic Engineering researchers from the university and several Welsh industry partners to develop a point

of care test which will be affordable and will allow results to be available in 20-30 minutes. Engineers at GX Group are designing and producing a set of device prototypes, BioMonde is producing the assay element of the test, and BIC Innovation has been providing guidance on regulatory requirements. Researchers have also been trialling a unique nasal swab printed on 3D printers within Cwm Taf Morgannwg UHB.

Due to its speed and portability, the new test could be used to help ramp up large-scale community testing with a short turnaround time for results. A point of care device could also offer a solution to people who perhaps live and work in more rural areas, as well as in specific care settings and industries to help detect outbreaks quicker and prevent further spread of the virus.



GX prototype image



“We have been developing our diagnostic testing platform for the last few years, so we know that it works well for other infections such as urine tract infections (UTIs). We have modified this very sensitive and precise technique which is based on proven molecular (LAMP) technology. This is a fluorescent detection of nucleic acid amplification, similar to standard qPCR methods, but at constant temperature. It was designed to be a simple, quick and cost-effective test, suitable for the diagnosis of a range of infections, so our work over the last few years has enabled us to quickly switch it to detect the underlying virus for Covid-19.”

Dr Jeroen Nieuwland
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Pontypridd

Wastewater provides insight into Covid-19 infection rates

Scientists at Bangor University are investigating what sewage can reveal about Covid-19 infection rates in different areas around the UK.

Knowledge of when and where coronavirus infections are occurring around the UK is vital in the fight to control its spread. Up-to-date information on when/where the disease is disappearing and when/where it is starting to re-emerge can also ensure that lockdown measures can be adapted accordingly.



"We now know that Covid-19 is mainly spread from person-to-person via respiratory droplets during coughing, and that it also has many symptoms which can vary widely from person to person, such as fever, headaches and coughing. Another symptom can be gastrointestinal pain. This occurs in many viral infections and Covid-19 is no different. We now have strong evidence that the virus can multiply in the intestines. So essentially, every time a person with coronavirus goes to the toilet, they pass the virus into the sewer network. Although the virus is inactive and non-infectious in the sewer network, and poses no risk to the environment, we can use this as a way to measure the abundance of Covid-19 in a whole city or town."

Professor David Jones

Lead Researcher
Bangor University School of Natural Sciences

Working with Welsh Water and United Utilities, scientists at Bangor University are monitoring the background levels of coronavirus in different areas. Their research has shown that tracing the virus, which is shed naturally, can provide an early warning of when certain areas may be approaching their next peak of Covid-19. Such early warnings are essential because symptoms can take up to a week to fully emerge, and some people show no symptoms at all when they are infected.

In recent months, the research team have worked with Welsh Water and United Utilities to take samples of water entering the wastewater treatment works, before measuring the levels of virus present. The time from sample collection to results is around 48 hours. The team can then

determine if the number of infections in the local area has increased, providing a potential early warning for the NHS.

This system is particularly suitable for large cities, as most UK urban centres are served by only one or two wastewater treatment works, providing a single integrated signal of millions of people in a single sample.

The team is now hoping to extend the project and work with other water companies. This would allow them to expand the surveillance network to other regions of the UK and to disseminate information so that people can be better protected against Covid-19.

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Bangor

Using dried blood spot testing technology for Covid-19

A Welsh collaboration has developed a low-cost test for Covid-19 antibodies using dried blood spots.

Dried blood spots (DBS) are most commonly used to test newborn babies for a variety of inherited diseases. They involve taking a tiny amount of blood from a skin prick and depositing this onto specialised filter paper. This is also known as the Guthrie card test, named after the American microbiologist Robert Guthrie who first described the technology in the 1960s.

Experts from the University Hospital of Wales, Cardiff University and the Welsh Blood Service have recently been collaborating to develop the use of DBS for testing Covid-19 antibodies.

A tiny amount of blood (one hanging drop per spot from a finger prick) is dropped onto a filter paper card, which is then allowed to dry and sent to the newborn screening service laboratory in the University Hospital of Wales. A disc from the card is then 'punched out' and the antibodies are released using a specialised liquid buffer. This sample is then tested using a laboratory platform. Cardiff University

has developed an ELISA (Enzyme Linked Immunosorbent Assay) antibody test, which has been optimised for DBS specimens and translated onto an NHS automated platform in the Immunology Department at University Hospital of Wales.

There are a number of reasons why this approach could prove useful in the Covid-19 pandemic. It only requires a finger prick sample of blood, rather like checking the blood sugar levels of a diabetic patient. This means that no healthcare workers such as phlebotomists, nurses or doctors need to be present in order to take blood, reducing the risk of possible Covid-19 transmission to or from healthcare workers, and the sample can easily be taken in the participant's home.

Also, the method does not require blood bottles or syringes, and the dried blood spot on the card is both stable and flat, allowing it to be sent through the post. This enables testing where distance presents a challenge and blood sampling resources are limited. If required, it can also be used by people who are shielding, and at a large scale. The send-in approach links

the testing to automated centralised laboratory platforms, which feed results directly into existing NHS pathology systems.

The cost of taking the sample is low, which is beneficial in scenarios where many samples are needed – for example when testing specific populations such as school teachers, nursing home residents or groups of healthcare workers in seroprevalence studies. The DBS testing pathway combines a low-cost blood sample collection technology with a cost-effective automated testing platform to enable large scale testing across significant geographical distances, which is particularly important in resource poor settings.

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Cardiff

New technology to disinfect ambulances

A team from Swansea University is developing a disinfection technology to decontaminate public spaces from Covid-19.



Members of the team have expertise in advanced oxidation techniques and novel building design (as part of the 'buildings as power stations' work undertaken by SPECIFIC), as well as water disinfection and surface treatments. When the Covid-19 pandemic began, the Swansea University colleagues, who had collaborated on projects in the past, started sharing ideas for disinfecting ambulances and discussing different gases that could be used for this purpose. They then also realised the need for an indicator technology to show the reach of the gas.

It is important to note that disinfection is different from cleaning, and the team is developing a new technology to disinfect invisible pathogens. Therefore, if a surface has been dirtied by liquids or solids, the technology is not designed to remove these.

Using a reactive gas to disinfect, instead of solutions or sprays, has an advantage because the gas is able to fill the entire space without any need for human cleaning intervention. The researchers are looking to optimise the treatment in order to fill the space and maximise pathogen disinfection. They are also working on applying the technology remotely.

The reactive gas fills the space, kills the pathogens and is then rendered harmless using

a destructive cycle. An indicator technology is in development to show where the reactive gas reaches. This means that viruses are not needed when testing the technology, which is significantly safer.

Initially the team responded to a challenge set by the Small Business Research Initiative (SBRI) Centre of Excellence and Welsh Ambulance Service to reduce the current turnaround time for disinfecting an ambulance and getting it back on the road after carrying a patient who could have Covid-19. With over 200 proposed solutions from across the UK, the Swansea University team was among the top twelve to secure funding and support. The rapid-release



"This project has benefitted from a truly team-based approach; bringing together chemical engineering, chemistry and materials science to attack the problem as quickly as possible."

Professor Peter Holliman
Swansea University

gas treatment for ambulances could remove Covid-19 contamination in under 20 minutes.

The researchers are now also developing the technology for use in schools. It has the potential to be applied in any public space, and they hope that the same approach could work with other pathogens in the future.

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Swansea

Leading the way on lung ultrasound to manage Covid-19

Research from Cardiff University is being used globally to inform pioneering use of lung ultrasound in the management of Covid-19 patients.

Lung damage can be a serious problem for patients with severe coronavirus symptoms. Key decisions – such as whether a patient should be admitted to hospital, moved from a ward to a high dependency unit and put on mechanical ventilation or taken off it – are usually informed by CT scans, chest X-rays or by listening to the chest. However, for infection control reasons, these cannot be used in the monitoring of Covid-19.



Cardiff University researchers have been exploring how ultrasound imaging, more commonly used in pregnancy or for muscle injury, can be used to assess and monitor lung damage. As the pandemic approached, the team gathered together early evidence and guidance for use of lung ultrasound in Covid-19 patients. They were the first to collate how ultrasound imaging can be used to look at lung tissue in order to map deterioration or improvement.



"We wanted to take the information that was flying around the research and clinical communities and make it more useful for clinicians, right at the beginning of the pandemic curve. Since then, lung ultrasound has emerged as critical to monitoring lung injury caused by Covid-19."

Dr Mike Smith
School of Healthcare Sciences
Cardiff University

A significant problem is that the standard assessment tool, the stethoscope, cannot be used with coronavirus patients because it forms a direct connection between the patient's skin and the clinician's face. As an alternative, lung ultrasound does not carry this risk, and the infection control processes needed when using it are relatively straightforward. It also provides real-time information on the state of the lung, giving it an advantage over other methods which take time to produce results.

Lung ultrasound can be carried out using handheld, portable units, as opposed to methods like CT scans which require large, bulky machinery. This means that lung ultrasound can be put to use in community settings including care homes and prisons, as well as in rural areas which have limited resources and are far away from hospitals.

It can be used to determine whether a person's condition is serious enough for hospital admission, potentially saving time and money for the NHS.

The researchers also outlined how different healthcare workers could be trained in use of lung ultrasound in order

to increase its availability. Usually, it is carried out by a relatively small but skilled workforce, comprised of intensivists (who specialise in the care of critically ill patients), anaesthetists, respiratory physiotherapists and advanced critical care practitioners and nurses. The team identified three workforces that could be upskilled to bring about a 50-fold increase in availability, including clinicians who have previous experience in lung ultrasound, sonographers who already have high-level imaging skills but may have a lower than normal workload, and experienced lung practitioners who don't usually work with lung ultrasound.

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Cardiff

T cell test to help understand Covid-19 immunity

Indoor Biotechnologies is developing a new type of test for Covid-19 which can identify the presence of virus specific T cells in blood.

Identifying people who have already been infected with the Covid-19 virus and become immune could have huge benefits for enabling society to safely return to normality. However, since the symptoms of Covid-19 can vary from person to person, and some people display no symptoms at all, reliable testing methods for prior infection and subsequent immunity are vital.

One way of determining whether someone has been infected with the virus is by looking for specific antibodies in blood samples, and multiple tests have already been manufactured to do this. However, there have been some doubts about the reliability of these antibody tests in determining whether a person has gained immunity.

Long-term protection against viruses comes not only from antibodies, but also from cells of the immune system called T cells, which play a critical role in controlling and eradicating viral infections.



A recent study at the Karolinska Institute in Sweden found that many people who had experienced mild or asymptomatic Covid-19 demonstrated T cell immunity to the virus, even if they did not test positively for antibodies. This indicates that public immunity could be higher than current antibody tests suggest.

The new test proposed by Indoor Biotechnologies is different because it focuses on T cells rather than antibodies. It may offer a better marker of immunity than other tests and could prove particularly helpful in vaccine development.

From a single tube of blood, the Cardiff-based company can identify the presence of T cells that respond to the Covid-19 virus, within 24 hours. This approach has the potential to be more sensitive and more reliable at determining immunity than antibody testing. To verify this, it will be tested on people who have already had the virus, recruited with help from the University Hospital of Wales, Cardiff.

The test may also be valuable during vaccine development, as it could be used to help identify whether an adequate immune response has been generated to protect people from Covid-19, and for testing how long that immune response remains.



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Cardiff

Blood oxygen monitors developed for Covid-19 patients

Researchers at the University of South Wales have developed an innovative blood oxygen monitor, after supplies of this key device became limited as a result of the Covid-19 pandemic.

The device, known as a pulse oximeter, was designed to be manufactured in Wales and break away from the standard oximeter supply chains, effectively eliminating future sourcing bottlenecks. Researchers at the University of South Wales developed it in collaboration with Panasonic UK and clinicians in Hywel Dda University Health Board.

The pulse oximeter clamps onto to a patient's finger, allowing clinicians to monitor the level of oxygen in the bloodstream and, importantly, the performance of their lungs. The university team identified key sources of measurement errors that occur, and in so doing were able to innovate a new highly accurate approach that can be implemented cheaply. The device provides high accuracies at lower oxygen levels, which is an essential requirement for effective Covid-19 treatment.

Normally this level of accuracy is only achievable with far more costly approaches, so the device has potential for deployment in community settings, enabling clinicians to remotely assess Covid 19 patients whilst they self-isolate at home. A clinician could remotely monitor the performance of a patient's lungs in order to determine appropriate and early life-saving treatment, such as CPAP to support breathing.

The team of researchers managed to turn around the concept from first principles to prototype in just two weeks. 20 prototypes

have been developed and have passed the rigorous manufacturing test EMC. The pulse oximeter has also been submitted for a fast-tracked MHRA (Medical and Healthcare products Regulatory Agency) approval, so that the NHS and other care providers can use it as soon as required.



"We wanted to be able to use our experience and knowledge of optoelectronics and engineering to develop something that could be of real use during the pandemic. After discussions, it became evident that we could really help the NHS by developing a superior low-cost pulse oximeter that could be manufactured locally, avoiding potential bottlenecks for demand, cutting delivery times and creating a new supply chain within Wales and the UK. We have not only achieved these goals, but have also delivered a significant innovative step that allows high performance at a low cost, thereby enabling widespread deployment in the community to save lives."

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Pontypridd



Digital platform enhances capabilities of coronavirus test

A platform created by Bond Digital Health will enhance a new Covid-19 test with digital connectivity and data capture technology.

Cardiff-based Bond Digital Health was planning to launch its platform for digitally connected diagnostic tests, called Transform, towards the end of 2020. However, when the global pandemic began, the company chose to fast-track the platform's development, so that it could be used in conjunction with a rapid test for coronavirus developed by Canadian firm Sona Nanotech.



The test is based on lateral flow technology, which is used in a wide range of human diagnostics, including for infectious diseases such as cholera, malaria and HIV. It can be administered at the point of use, with no need for skilled technicians or additional laboratory equipment. The common pregnancy test used by millions of people each year is an example of a lateral flow test.

In terms of current testing methods for coronavirus, certain tests (such as PCR tests) can tell whether someone is carrying the active virus, but these require laboratory analysis so

they are expensive and take time to produce results. Meanwhile, portable antibody tests (which are lateral flow tests) are significantly cheaper and quicker to use, but they generate more limited information. Many of the rapid tests are not specific or sensitive enough to detect Covid-19, because they look for antibodies which are only identifiable post-infection.

The new test is designed to combine the best of both types. It is a direct antigen test that looks for a specific coronavirus protein. As a lateral flow test it is cheap, quick and easy to use, but unlike most antibody tests it can tell if someone is carrying the active virus in real-time, at the point of testing.

Sona Nanotech is getting a basic version of the test out quickly to help with large scale testing. Bond Digital Health is working on the

next stage, which is a digitally enabled test, connected to the cloud and the web. This will enable scientists to collect additional data on blood groups, ethnicity, age, underlying health conditions and location, instantly map those results against the results of the test and then share the data with relevant organisations.

Transform is a platform with end-to-end connectivity, which transforms traditional lateral flow devices into web connected diagnostics with accessible, shareable data. Adding this to the virus test will allow valuable test data to be securely captured, stored, analysed and shared. This could ultimately help authorities to monitor and therefore control the spread of the outbreak.

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Cardiff



Detecting coronavirus with breath analysis technology

A breath analysis device developed by IMSPEX Diagnostics is undergoing trials to determine its ability to detect coronavirus.



Gas Chromatography-Ion Mobility Spectrometry (GC-IMS) is a relatively new technology which analyses Volatile Organic Compounds (VOCs) in a sample. These are essential compounds which are responsible for smells and aromas.

Abercynon-based company IMSPEX Diagnostics has developed several devices that make use of GC-IMS technology, including a device called BreathSpec for medical applications. It uses GC-IMS technology to analyse VOCs in human breath and detect certain VOCs associated with disease and infection.

The device is designed to be used at the point of care and produce fast results. A patient breathes into a mouthpiece to provide a breath sample, and the result is then generated in less than five minutes. Other devices are able to take the breath sample at the point of care, but the sample must then be transported to a laboratory in order to be analysed. This can significantly increase time and cost of diagnosis. The device is portable



As part of a wider project to reduce over-prescribing of antibiotics and combat antibiotic resistance, the technology was recently used to assess its ability to distinguish between viral and bacterial infections. The results are promising and have enabled the company to further develop this application.

which means it can be easily transported around wards from patient to patient and can also be used in the community setting.

IMSPEX now hopes that the technology can be deployed during the global pandemic to identify VOCs associated with Covid-19 infection. It offers a non-invasive approach, which does not require nasal or throat swabbing. Once a patient has exhaled into the mouthpiece and provided a breath sample, the system can provide results in just a few minutes with no need for

analysis in a laboratory, allowing for rapid diagnosis and treatment.

The company identified the potential of its technology for coronavirus testing early on and has partnered with several NHS sites and universities, including the Royal Infirmary of Edinburgh, Loughborough University, Leicester Royal Infirmary and University of Warwick. Trials are still ongoing, but early results are encouraging for the use of the BreathSpec to detect coronavirus now and for its use in other future pandemics.

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Abercynon

Biocidal face masks to tackle the global shortage

Hybrisan is developing a new generation of face masks for frontline workers.

The Covid-19 pandemic has created a shortage of anti-viral products such as sanitisers and Personal Protective Equipment (PPE). This is an issue both in the short term, due to the huge increase in demand, and in the long term as the crisis has exposed the fragility of international supply chains.

Hybrisan, which featured in Advances 91, manufactures liquid sanitiser and uses nanotechnology to produce an advanced material, with the sanitiser incorporated, for use in PPE. The liquid sanitiser developed by the company is effective in killing coronavirus without alcohol.

SARS-CoV-2, the coronavirus which causes Covid-19, is an enveloped virus. The viral DNA and RNA is protected by a lipid membrane. Without the lipid membrane, the DNA and RNA contained within the virus cannot survive and cause infection. By breaking down the relatively sensitive lipid membrane it is possible to deactivate the virus and eliminate the threat of disease. This can be done in a



"It has been well documented that nanofibrous material protects against harmful bacteria. We have studied these properties in depth and have now developed products that are proving to be extremely effective against both harmful bacteria and viruses. Our expertise in this field has prepared us for the challenges presented by the coronavirus pandemic and we are pleased to have been able to develop products which will help."

Dr Lee Bridgeman
 CEO
 Hybrisan

number of ways - through hand washing, bleaching surfaces, using high alcohol sanitisers, and using aqueous sanitisers with antimicrobial properties like those developed by the Port Talbot-based company.

The company has been using an electrospinning technique to create

antimicrobial fibres, which can repel or kill harmful bacteria and viruses. Electrospinning uses a high voltage to produce fibres from a polymer solution. A current is passed through the solution causing it to be accelerated towards a collector. This allows the structure to be randomly arranged into a delicate solid state. These ultrafine fibres, often referred to as nanofibres, can then be used as a nonwoven fabric.

The resultant fabric can be used to make face masks which are both biocidal and reusable, providing an alternative to ordinary materials currently in use. This will contribute to improving safety for frontline workers and reducing the global shortage of face masks.

Hybrisan is currently testing and developing its electrospun nanofibre material for use in face masks, and a grant has allowed them to accelerate the process. Initial launch of the next-generation face mask is expected in 2020, with full global production to start in early 2021.



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Port Talbot

Databank enables vital health data research

An extensive health data resource built by Swansea University is being used to inform vital research into Covid-19.



SAIL Databank has proven useful for Covid-19 research because it can monitor the impact of a wide range of exposures and outcomes on the entire population. It is possible to track the development of health conditions in individuals and within households and multi-occupancy residences such as care homes, as well as in organised settings like schools.

Based at Swansea University Medical School, SAIL Databank brings together anonymised person-level data from a variety of health and other public services/organisations, providing this as a resource for researchers via a secure portal.

This is the culmination of a decade of innovation by a small team of data scientists, information governance experts and IT professionals at Swansea University, with support from Health and Care Research Wales. Their mission was to create a secure platform which provides the widest possible access to linked data, without compromising data and privacy protection.

Among all of its data sources, it contains 100 per cent secondary care and 80 per cent primary care coverage for the Welsh population, delivered through a partnership with the NHS Wales Informatics Service (NWIS).

It also makes it possible to monitor the development and spread of diseases, and evaluate the impact of exposures and the effects of treatments on outcomes. Data can be made available to researchers as quickly as 48 hours, even at present, when the team is seeing as many data access requests from researchers in one week as they would more commonly see in a typical month.

SAIL Databank is now used as the data repository for the ZOE COVID-19 Symptom Study app, in partnership with BREATHE – the Health Data Research Hub for Respiratory Health. It is also a key partner in the COVIDENCE UK study, enabling numerous Covid-19 related studies to take place.

The team is part of the Health Data Research (HDR) UK consortium, which was set up to unite the UK's health data and make it available for research, and this consortium is now working to provide data access for a high volume of Covid-19 research studies. SAIL Databank is being used for research covering themes including: emergency response planning; the impact of the pandemic on mental health; clinical trials comparing treatment pathways; the link between ethnicity and the severity of Covid-19; connecting data to Covid-19 testing programmes; and the impact on society's most vulnerable groups.

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