



Covid-19 and drug resistance

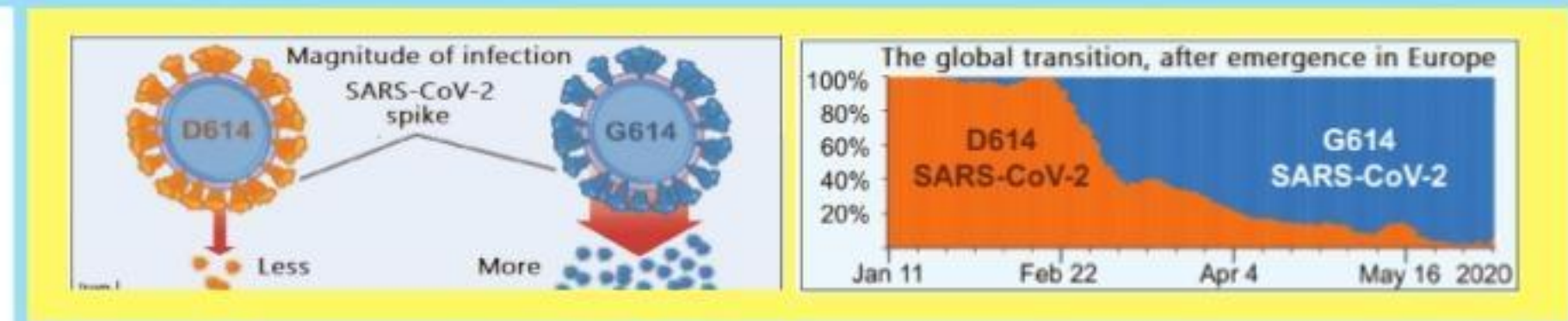
The novel coronavirus appears to be a moving target

ANANTHANARAYANAN

While Covid-19 brings the world to its knees, great hope is pinned on a vaccine being found. A disturbing thought, however, is that the virus may undergo changes and slip out of the net the vaccine throws around it.

The journal *Cell* carries a paper by scientists from Duke University, North Carolina; Los Alamos National Laboratory, New Mexico; La Jolla Institute in California and the University and institutes in Sheffield, UK, which reports that there has been a positive shift in the form of Sars-CoV2, the virus that causes Covid-19, since the early months of the outbreak. Much of the work of developing vaccines or testing methods are based on the envelope, or outer features, of the initial Wuhan virus, the paper says. Changes in the virus in the course of its spread worldwide could hence affect the utility of interventions which are based on how the body reacts to the exterior, physical features of the virus.

The researchers, on behalf of the Sheffield Covid-19 Genomic Group have hence developed a bioinformatics-based system to monitor evolution of the virus over time, an "early warning" strategy to assess and improve therapy and testing, to keep up with



changes in the virus.

The proliferation of a virus depends on its being able to enter living cells, so that they use the cells' resources to multiply. The external features of the virus, which enable its entry, are thus maintained, in the course of virus multiplication, as new viruses that lack these features would not be able to propagate. At the same time, the body's defence is also designed according to the features of the virus exterior. Chance variations in the surface, which do not affect the virus' ability to infect cells, could hence help it evade body defences. Viruses that have these variations would then survive the defences and emerge as a new, dominant strain.

Coronaviruses, which cause the common cold or influenza, are known to undergo these changes. This is what explains the persistence of colds among humans, and the need for a new influenza vaccine every few years. While

the coronaviruses that caused Sars or Mers did not last long, the high infectivity and spread of Sars-CoV2 makes it likely to grow and thrive in new forms. The "early warning" method of the research group makes use of the database of the Global Initiative for Sharing All Influenza Data, a collaboration of laboratories that sample and analyse the Sars-CoV2 virus, worldwide.

Based on ΔH_0 data, the first significant change the group discovered was a change in a specific part of the genetic sequence associated with a feature, the D614 Spike of the original virus. The Spike was found changed to D614G, referred to as the "G glade", as opposed to the "D glade". The G variety first appeared in March 2020, and was "rare globally," at the time. But it rapidly multiplied and now dominates the Sars-CoV2 population.

The human body defences, fortunately, are as effective against the "G" variety of the virus as against the "D"

variety, perhaps more effective, the paper says. The disease it causes is also not more severe than that of the "D" variety. The "G" variety, however, multiplies faster – and is hence found in more abundant titre, or concentration. "All the more reason to use the mask," a press release from La Jolla Institute says.

Remdesivir

In the same week as the paper in *Cell*, the journal *Scientific Reports* carries an editorial on the most effective drug for Covid-19, so far, whose effect is based on the mechanism that helps coronaviruses change and stay ahead of body defences.

The National Institutes of Health, the foremost medical research agency in the US, has announced initial findings that the drug, Remdesivir, manages to reduce the time for recovery from Covid-19 by 31 per cent, compared to a placebo. While a more extensive study has been undertaken, several countries,

including India, have authorised using remdesivir to treat patients with severe disease.

Remdesivir is a "transcriptional inhibitor", which is to say that it acts by coming in the way of the virus by making use of its own genetic information. The action of all cells, and viruses, is controlled by the DNA, a molecular coding of all the proteins that the cell or virus can produce. The way it works is that parts of the coiled DNA molecule are opened and segments copied, or transcribed, so that the segment can be made use of. The DNA consists of a pair of complementary strands coiled around each other, so that either half can rebuild the other, if they are separated, which enables replication. The copies taken for making proteins, however, are single-stranded segments, called RNA, a little different from DNA.

This action of copy making takes place with the help of an enzyme called *RNA polymerase*. RNA polymerase plays a vital role in converting the code in the DNA into information to build proteins, and is present in almost the same form in the cells all the way from single-celled bacteria to humans. One would hence expect that the enzyme would also work for Sars-CoV2 when it gets into the cell. But coronaviruses are different as they contain no DNA. In its place, they have a strip of RNA, a single strand that codes only for the proteins that make up the spike on the outer cover.

For expression of the viral RNA, and for its replication, we need another enzyme, the RNA-dependent polymerase, or *RdRp*. Sars-CoV2 as well, since it is a coronavirus, needs *RdRp* to replicate. And for their best survival, RNA viruses have evolved so that *RdRp* is "error" prone – and creates some new RNA that contain changes – which may perish or overcome body defences. In the latter case, they would thrive, and grow into new, "resistant" strains.

The drug, Remdesivir, has a component that replaces a unit in RNA and confuses the build process to terminate prematurely. The result is that the Sars-CoV2 is not able to proliferate and initial findings are that the severity of the disease declines, with faster recovery.

Remdesivir was originally developed to deal with the Ebola pandemic, but was found not to be effective. The first effort, in China, to see if it would fare better with Sars-CoV2, could not be completed because Covid-19 came under control and there were not enough patients. The trials were hence taken up in Europe, with encouraging results in the preliminary stages. Other, analogous preparations may also prove effective, both as curative agents and to find ways around drug resistance as well as the fast replication of Sars-CoV2.

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PLUS POINTS

Sign language glove



Bioengineers have designed a glove that is able to translate American Sign Language to speech in real time.

The glove has thin, stretchable sensors inside, which run to the fingertips. These sensors are able to pick up motions and finger placement through electrically conducting yarns. Those sensors are then connected to a small piece of circuit board – approximately the size of a coin – that users wear on their wrists.

As such, when people move their hands and fingers to sign words, the glove is able to translate the individual letters, numbers, words and phrases into spoken words. Extra sensors can be added to the face, between the eyebrows and on the sides of the mouth, to capture facial expressions.

The actual translation is done through a smartphone app, which uses a custom machine-learning algorithm to turn gestures into the letters, numbers and words. The system recognises 660 signs, which includes each letter of the alphabet and the numbers from zero to nine. It can translate at a speed of one word per second.

A commercial version of this technology would require more vocabulary and a faster translation time. The University of California, Los Angeles has filed a patent on the glove.

"Our hope is that this opens up an easy way for people who use sign language to communicate directly with non-signers without needing someone else to translate for them," said Jun Chen, the principal investigator on the glove. "In addition, we hope it can help more people learn sign language themselves."

Zhihao Zhao, Kyle Chen, Songlin Zhang, Yihao Zhou and Weili Deng, from UCLA, authored the study that developed the glove, alongside Chen. Jin Yang, of China's Chongqing University, also authored the study.

The benefits of the glove are its portability and weight. Previous wearable devices offered similar capabilities, but were heavy and impractical to wear. This new design is far lighter, and the polymers are inexpensive – as are the electronic components.

However, some deaf researchers have criticised the development. "The tech is redundant because deaf signers already make extensive use of text-to-speech or text translation software on their phones, or simply write with pen and paper, or even gesture clearly," said Gabrielle Hodge, a deaf researcher from the Deafness Cognition and Language Research Centre at University College London, to CNN. "There is nothing wrong with these forms of communication. It would be so much easier if tech focused on user-driven and user-centred design in the first instance, rather than dreaming up 'solutions' they think will fix all the problems in the world."

—The Independent

Largest rocky planet



A rocky planet that is 39 times as massive as Earth has been spotted orbiting a distant star at breakneck speed, with astronomers concluding it may be the surviving core of a planet once perhaps larger than Jupiter that was stripped of its gaseous atmosphere.

Researchers said last week that it is the largest rocky planet ever discovered and would be the first planetary core ever found, offering a unique opportunity to better understand the interiors of gas giants like Jupiter, the largest planet in our solar system.

The planet, called TOI-849b, orbits a star a bit smaller and cooler than the Sun, located 730 light years from Earth. Gas giants are composed of a solid core surrounded by a vast atmosphere mostly of hydrogen and helium.

"This planet could have been a gas giant like Jupiter, which then lost its outer envelope through some violent evolution. This could be because it collided with another planet towards the end of its formation, or later ventured too close to its host star and was stripped of its atmosphere," said astronomer David Armstrong of the University of Warwick in England, lead author of the research published in the journal *Nature*.

—The Straits Times/Ann

ANNA JORGENSEN

Experiencing Nature is likely to be a lifeline for many in this time of Covid-19. This doesn't just mean visiting parks or iconic locations outside urban areas. Our "Improving Wellbeing through Urban Nature" research suggests that everyday Nature, including people's gardens, views of trees and skies from the window, potted plants, birds, animals or even plants growing through cracks in the pavement may be just as important as visits to special places.

Nature can change the way we are feeling, and influence how we think about ourselves and our lives. Exposure to Nature affects our mental health through multiple pathways -- through a process known as psychological restoration, physiological changes in our bodies, social activity and feelings of connection to something larger than ourselves.

Psychological restoration is a complex process with different stages. Research has found that when they are experiencing Nature, most people consistently report feeling relaxed, a sense of getting away from their everyday lives, regaining their vitality and having an opportunity to get their problems into perspective and feel more hopeful. Different psychological models explain the process.

One model suggests that people get mentally fatigued through having to pay attention to their work and other activities of daily living. Nature provides lots of opportunities for "soft fascination" – things that are inherently absorbing, encouraging to pay attention to them without having to make a conscious effort. They might include sensory impressions from things like birdsong, raindrops, smell of wet earth, feel of wind or sunshine, and the patterns and rhythms of leaves, trees and cloud formations. The research suggests that even a few minutes of "soft fascination" in Nature leave people feeling less stressed and mentally refreshed, allowing them to refocus on their problems and tasks.

Another model suggests that exposure to Nature leads to more positively toned emotional states accompanied by positive physiological changes such as reduced heart rate and blood pressure. This might be experienced as moving from feeling exhausted and irritable, to restful and optimistic.

Other developing fields of study confirm the close relationships between



Reconnecting with Nature

Green spaces can change the way we are feeling, and influence how we think about ourselves and our lives

people and their surroundings. Research has shown that people with prolonged exposure to natural surroundings, for instance those who live in areas with lots of greenery and green spaces, have healthier daily fluctuations in their levels of the stress hormone cortisol. It is likely to result in people feeling less stressed and reducing their vulnerability to illness and disease. Another current area of research is exploring the relationship between the microbiome and people's physical and mental health. The microbiome consists of tiny microscopic organisms such as bacteria, which inhabit our environments and live inside or on the human body. One theory suggests that in order to stay healthy, the human body needs exposure to these organisms or "old friends" in their environment. It claims that many of the places we inhabit have too few of these organisms, reducing our exposure to them and compromising our immunity as a result. Having

contact with biodiverse microbiota in natural environments is likely to help boost the human microbiome.

While it's perhaps easier to accept that our physical health might be influenced by our own personal microbiome, like through the "healthy bacteria" in our gut, it's fascinating to learn that evidence also suggests that mental health and wellbeing might be positively affected by these tiny organisms.

Humans are generally social in nature, needing connection with other people in order to thrive, and there is also evidence that green spaces support our social relationships. They provide a space away from the stresses and strains of daily life where we can spend leisure time with friends and family.

Research has also found that even for people who are less socially-minded, urban green spaces provide areas of refuge and retreat, where people can experience solitude, whilst also being able to observe others and feel part of a

community from a safe distance. Research interest into the importance of "Nature connection" has also grown recently. Wellbeing, or feeling good, is about having positive experiences, but also about feeling that one's life is meaningful. Many people get this sense of meaning from feeling connected to Nature – something larger than themselves that carries on no matter what.

Lockdown and social distancing places incredible strains on us. Nature provides a way of alleviating that stress and taking time out from what might be a crowded and trying domestic or work situation. Green spaces are likely to be safer than indoor environments as the indications are that the virus is less likely to spread in unconfined spaces outdoors.

On the contrary, as explained above, spending time outdoors might actually help us boost our immunity to illness and disease through contact with the beneficial organisms found there.

