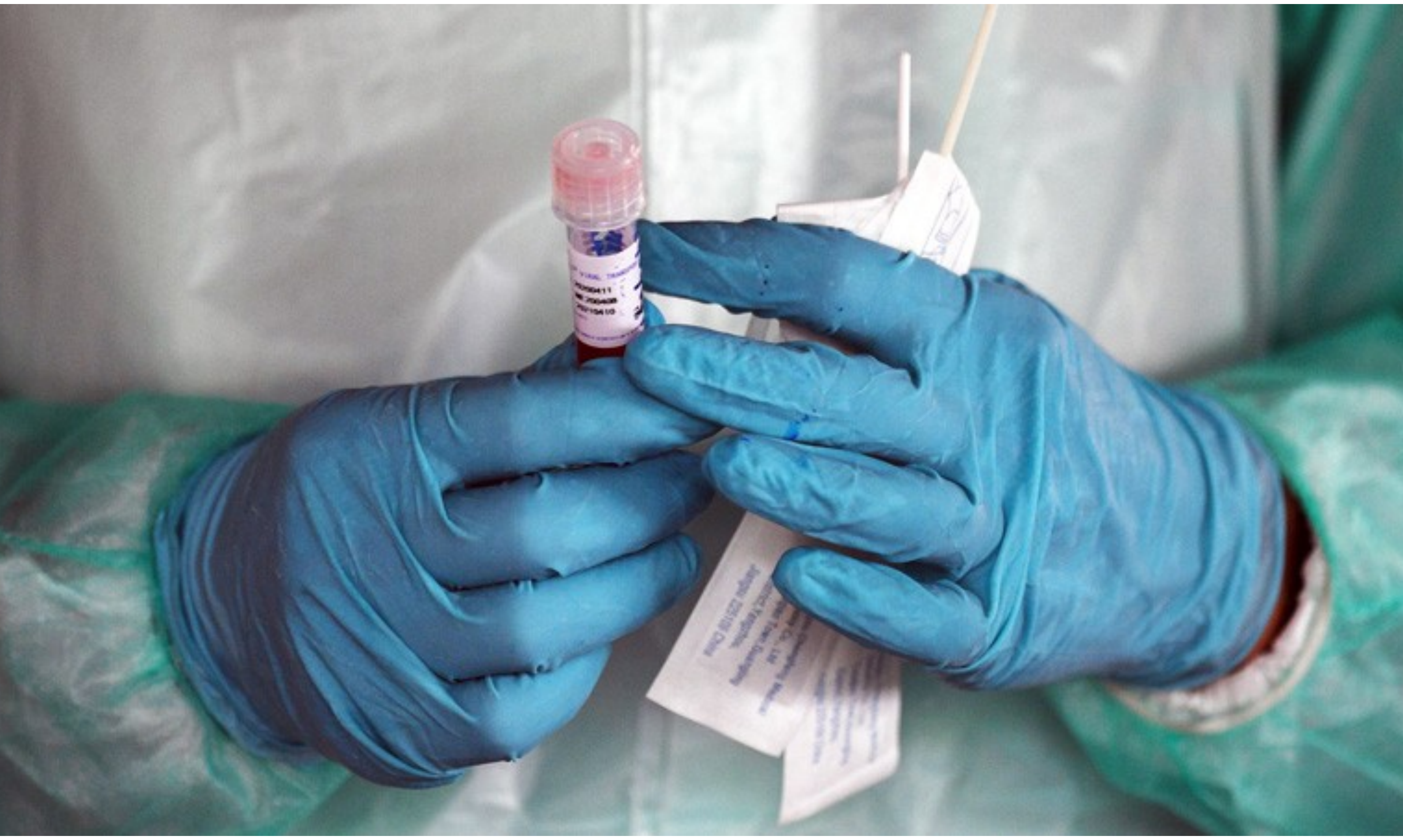
NEWS · 27 APRIL 2020

Pick of the coronavirus papers: Hospital toilets can be a hotspot for airborne viral RNA

Nature wades through the literature on COVID-19 so you don't have to.



A health-care worker preparing to test people for SARS-CoV-2 holds throat swabs, now a scarce and sought-after resource. Credit: Mohd Rasfan/AFP/Getty

Fresh findings about SARS-CoV-2 and the disease it causes.

27 April — Hospital toilets can be a hotspot for airborne viral RNA

The new coronavirus's RNA can travel through the air, and might spread by way of small

CoV-2 RNA in aerosols — fine airborne particles — at two hospitals treating people with COVID-19 (Y. Liu *et al. Nature* https://doi.org/10.1038/s41586-020-2271-3; 2020).

The team detected elevated levels of viral RNA in locations such as a small toilet used by patients, and staff changing rooms. No viral RNA was detected in staff rooms after they had been disinfected. Low to undetectable levels were found in the hospitals' well-ventilated patient wards.

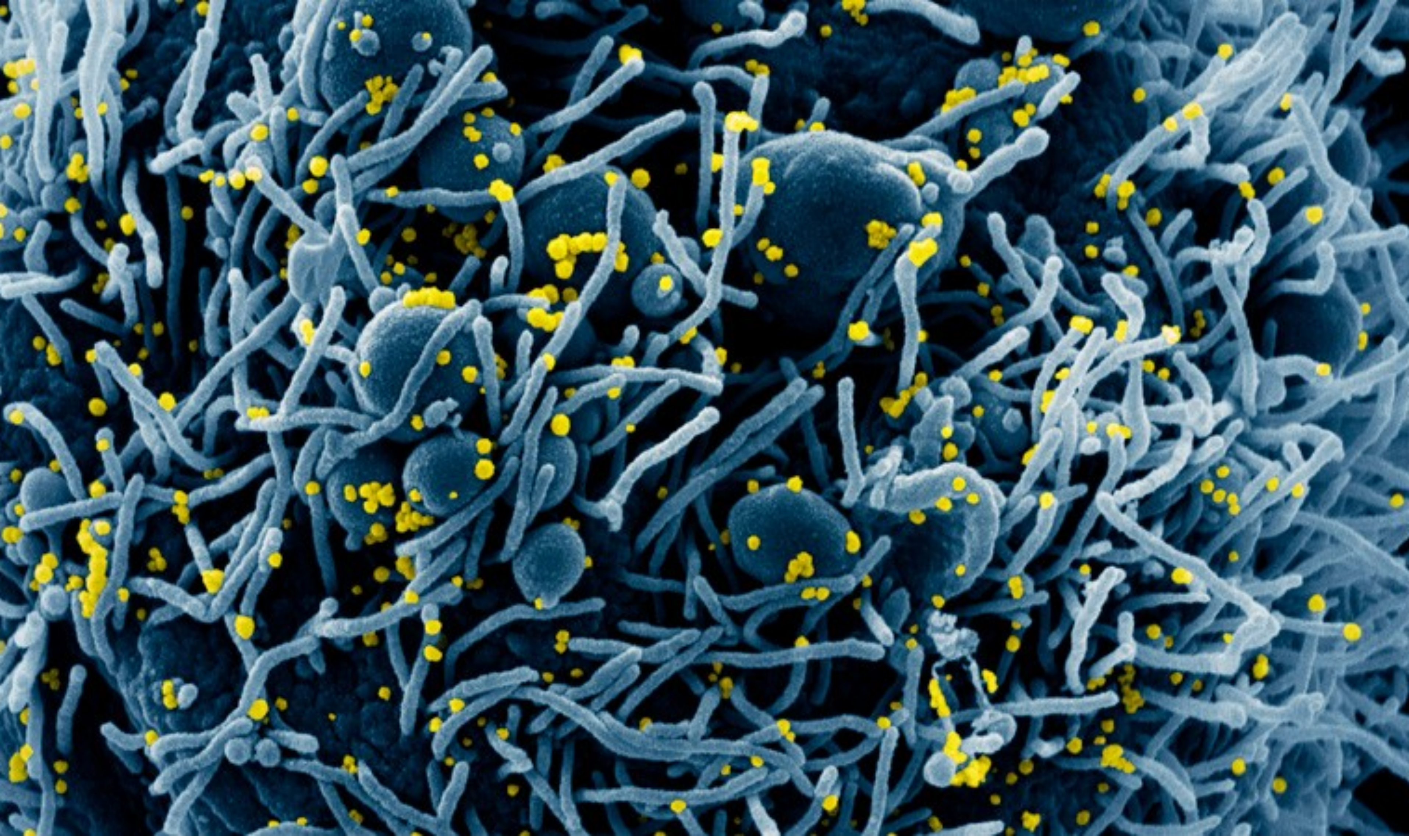
The presence of airborne viral RNA suggests that SARS-CoV-2 has the potential to spread by way of aerosols, the researchers say. They suggest that measures such as routine disinfection and better ventilation could help to control the virus's spread.

24 April — Spit could be the solution to testing shortages

A person's saliva accurately reveals whether they are infected with SARS-CoV-2, a finding that could make tests for the virus safer and more widely available.

The gold-standard test for coronavirus infection requires a long swab to be rubbed against the back of the throat. But such swabs are in short supply, and swabbing can prompt people to cough or sneeze, potentially launching a barrage of viral particles.

Anne Wyllie at the Yale School of Public Health in New Haven, Connecticut, and her colleagues collected both saliva and throat samples from people hospitalized with COVID-19 (A. Wyllie *et al*. Preprint at medRxiv, http://doi.org/ggssqf, 2020). The team's testing did not detect the virus in some patients' throat-swab samples — but did detect it in the same patients' saliva samples. Saliva testing also showed that two health-care workers who felt fine and had negative throat tests were actually infected.



A human cell (blue; artificially coloured) infected with SARS-CoV-2 (yellow). Credit: NIAID/NATIONAL INSTITUTES OF HEALTH/SPL

23 April — Intensive testing finds a small town's many silent infections

A large proportion of people with COVID-19 have no symptoms, according to research in a small Italian town.

On 21 February, the town of Vo' reported Italy's first COVID-19 death, leading authorities to ban movement in the town and end public services and commercial activities there for two weeks. Andrea Crisanti at Imperial College London and his colleagues swabbed almost every resident of Vo' for viral RNA at the beginning and end of the lockdown.

The team found that some 43% of the people infected with SARS-CoV-2 in the town reported no fever or other symptoms (E. Lavezzo *et al.* Preprint at medRxiv http://doi.org/ggsmcj; 2020). The researchers observed no statistically significant difference in potential infectiousness between those who reported symptoms and those who did not.

Asymptomatic and pre-symptomatic individuals have a key role in COVID-19 transmission, which makes it difficult to control the disease without strict social distancing, the authors say.

22 April — A vaccine candidate shows early success in an animal trial

An experimental vaccine protects monkeys from infection with the virus that causes COVID-19.

A team led by Chuan Qin at the Peking Union Medical College in Beijing injected rhesus macaques (*Macaca mulatta*) with three doses of a vaccine comprised of chemically inactivated particles of SARS-CoV-2 (Q. Gao *et al*. Preprint at bioRxiv http://doi.org/dskt; 2020). Eight monkeys were then intentionally exposed to the virus.

All four monkeys given a high dose of the vaccine had no detectable virus in their throat or lungs seven days after exposure. Monkeys that received a lower dose of vaccine showed some signs of coronavirus infection — but their levels of virus were much lower than in exposed animals that received no vaccine. This month, the company developing the vaccine received approval to start human safety trials on it.

A man with COVID-19 is treated at an intensive care unit in Rome. Credit: Antonio Masiello/Getty

20 April — How Hong Kong stemmed viral spread without harsh restrictions

Hong Kong slowed the spread of SARS-CoV-2 through a combination of intensive surveillance, quarantining and social distancing without relying on severe measures used elsewhere.

In January, the authorities in Wuhan, where the coronavirus outbreak began, halted travel out of the city in an attempt to control the spread of the virus that causes COVID-19. But Hong Kong relied on a programme that included widespread testing, quarantining of those who had been in contact with infected people, and distancing measures such as school closures. When Peng Wu at the University of Hong Kong and her colleagues surveyed residents in early March, 99% said they wore a mask in public and 85% said they avoided crowds (B. J. Cowling *et al*. *Lancet Public Health* http://doi.org/dsfw; 2020).

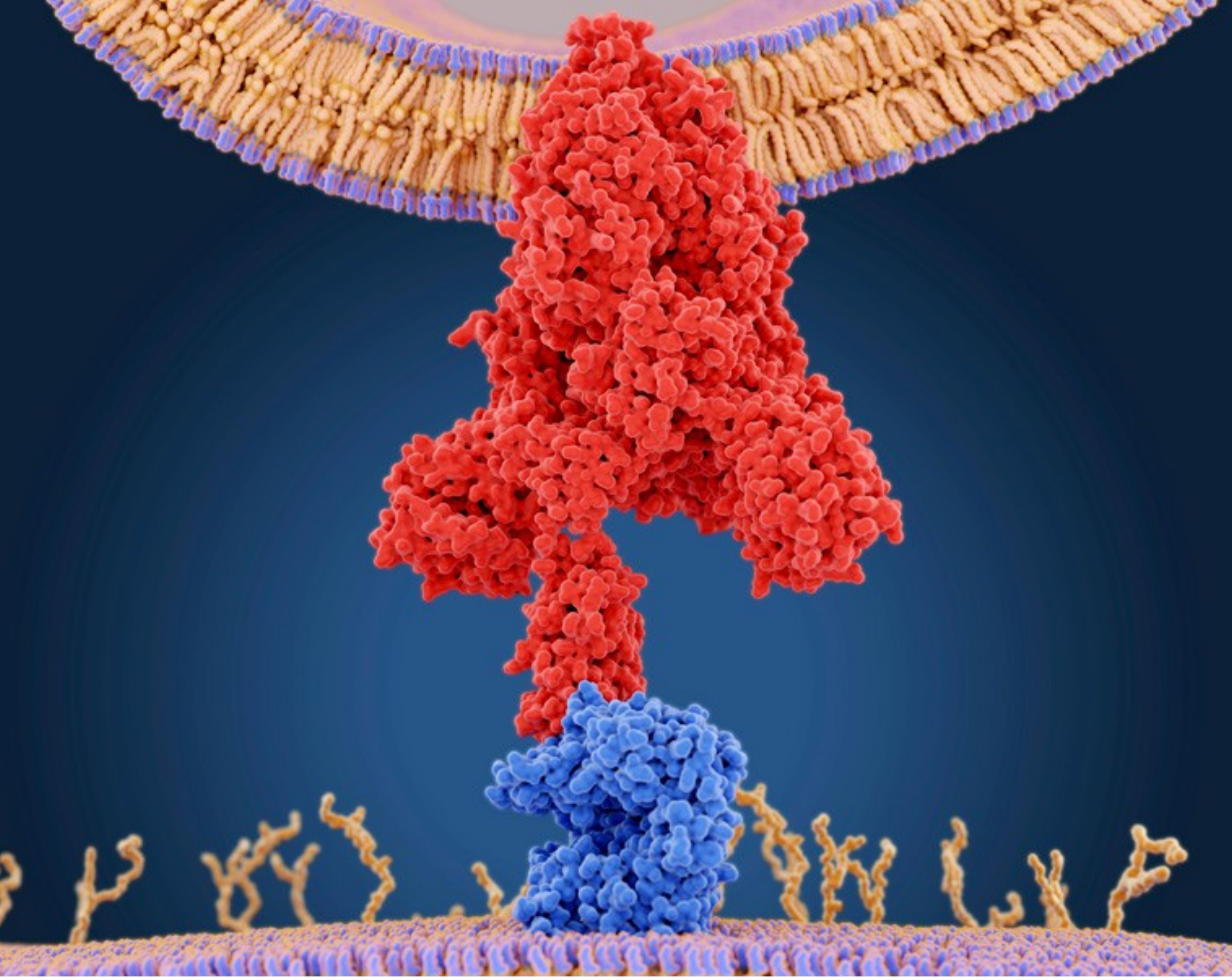
The combination of public behavioural changes and government measures kept the virus's spread relatively low in Hong Kong during the period to the end of March, the team found.

17 April — Vaccine from viral spikes holds promise

A key portion of a coronavirus protein could form the basis of a safe and effective vaccine.

Coronavirus particles bristle with spiny 'spike proteins'. A portion of the spike called the receptor-binding domain recognizes and attaches to a molecule found on the surface of many human cells, allowing the viral particle to gain entry into those cells.

Hyeryun Choe and Michael Farzan at the Scripps Research Institute in Jupiter, Florida, and their colleagues immunized rats with fragments of the spike's binding domain (B. D. Quinlan *et al*. Preprint at bioRxiv, http://doi.org/ggrs5t; 2020). In response, the rodents' immune systems made antibodies that can recognize coronavirus and prevent it from infecting cells.



One of the spike proteins (red) on a SARS-CoV-2 particle grabs a receptor on a cell. Credit: SPL

Further experiments suggested that these antibodies are unlikely to make host cells more susceptible to coronavirus infection — one of the main safety concerns for vaccines.

16 April — Ski buffs helped to seed coronavirus in Iceland

Holidaymakers returning from ski trips to the Alps helped to bring the coronavirus to Iceland.

In late January, Kari Stefansson at deCODE Genetics-Amgen in Reykjavik and his colleagues began testing for SARS-CoV-2 among Iceland residents at high risk of exposure to the virus, such as travellers to China (D. F. Gudbjartsson *et al. N. Engl. J. Med.* http://doi.org/ggr6wx; 2020). Some 13% of the 9,199 people tested by early April were infected. The team sequenced viral RNA from people who tested positive and found that some of the strains had probably originated in Austria or Italy, which both have Alpine ski resorts.

Tests in the second half of March on more than 2,000 randomly selected individuals found that only 0.6% were infected. The researchers say their analysis suggests that measures to contain the virus through testing, contact tracing and quarantining have been successful in Iceland.

A healthcare worker dressed for a shift in the COVID-19 intensive care unit in Lisbon. Credit: Patricia De Melo Moreira/AFP/Getty

15 April — Relief from social distancing could unleash the virus anew

Cases of COVID-19 are likely to surge after current social-distancing measures are eased, according to models.

Yonatan Grad, Marc Lipsitch and their colleagues at the Harvard T.H. Chan School of Public Health in Boston, Massachusetts, modelled the spread of coronaviruses in places that have temperate climates, such as the United States. The results helped the team to predict the spread of SARS-CoV-2, the coronavirus that causes COVID-19 (S.M. Kissler *et al*. *Science* http://doi.org/drz3; 2020).

The researchers found that if SARS-CoV-2 spreads more efficiently in some seasons than in others — as influenza virus does, for example — the peak number of COVID-19 cases after social distancing ends could be larger than the peak number without any social distancing at all. That's because distancing measures leave a high proportion of people susceptible to infection, leading to a spike of disease if viral transmission ramps up late in the year.

If human immunity to SARS-CoV-2 wanes over the course of a few years, the virus is likely to cause repeated outbreaks in wintertime, the authors say.

15 April — Common sequencing technique could speed large-scale diagnosis

A standard genomic-analysis method that can sequence tens of thousands of DNA samples in a day has been adapted to detect the virus that causes COVID-19.

In a testing protocol proposed by Jonathan Schmid-Burgk at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, and his team, every sample being tested for SARS-CoV-2 would be tagged with a unique DNA sequence that would serve as a biological barcode (J. L. Schmid-Burgk *et al*. Preprint at bioRxiv, http://doi.org/drzc; 2020). High-speed sequencing instruments common in research laboratories around the world could then be used to analyse as many as 100,000 DNA samples at one time.

The authors anticipate that if clinical testing validates the method, then millions of samples could be analysed per day at each sequencing site — a far more efficient output than that of current testing techniques.

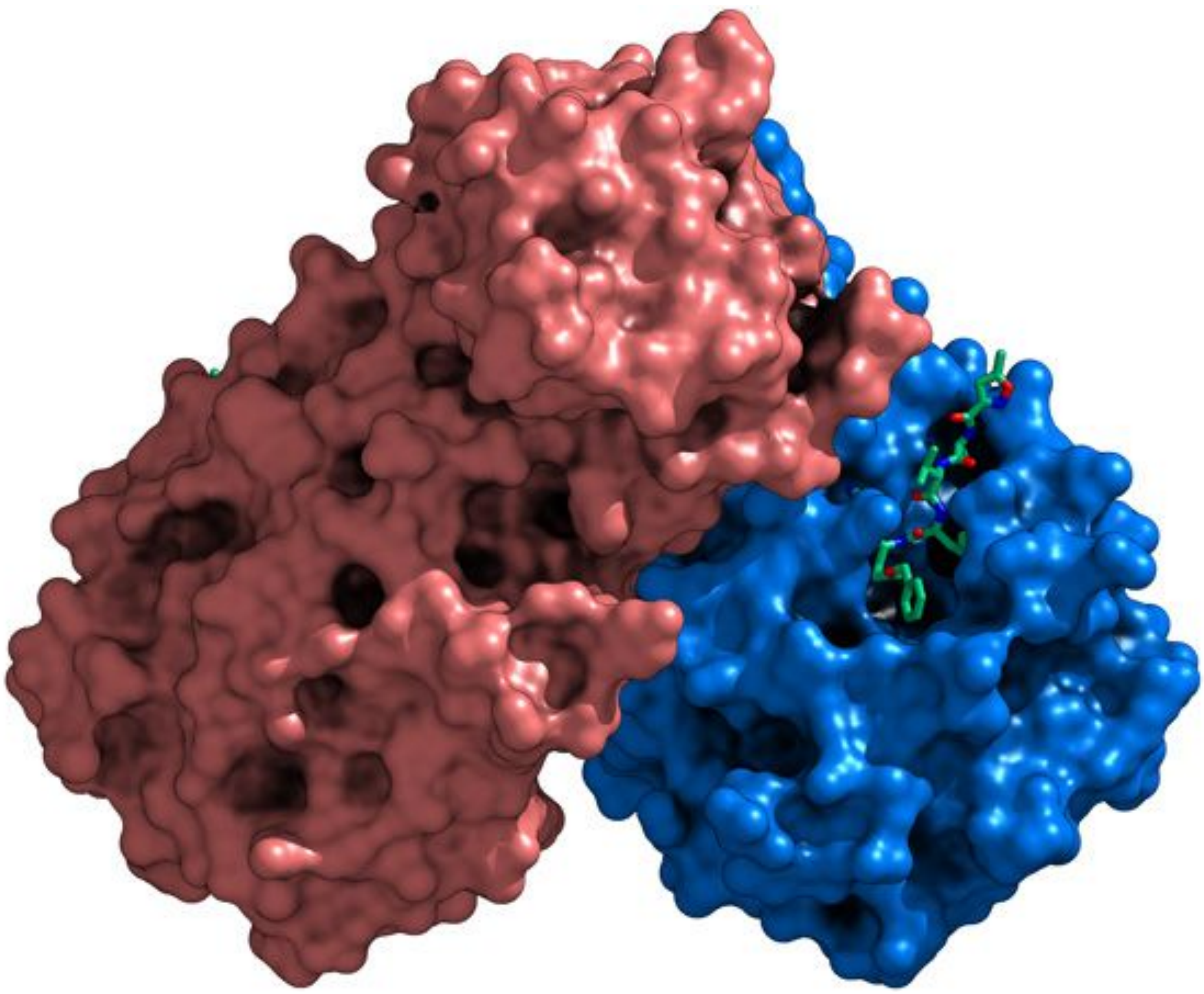
Correction: An earlier version did not include the name of the paper's corresponding author, Jonathan Schmid-Burgk.

10 April — A viral enzyme's structure points to possible drugs

Scientists have detailed the crystal structure of one of SARS-CoV-2's key proteins, an enzyme called a protease that the virus needs to replicate within our cells.

Hualiang Jiang, Zihe Rao and Haitao Yang at ShanghaiTech University in China and their colleagues deposited the structure in a protein data bank two months ago, and have since used it to help them identify compounds that inhibit the protease (Z. Jin *et al. Nature* https://doi.org/10.1038/s41586-020-2223-y; 2020). The team's screening revealed several powerful viral inhibitors, including ebselen, whose safety has already been tested in people.

These inhibitors work by infiltrating a hollow in the protease. Proteases found in other coronaviruses have a similar hollow, raising hopes that a single compound might help to treat a wide variety of diseases caused by coronaviruses.



One of SARS-CoV-2's key enzymes consists of two units (blue and red; artist's impression) and includes a hollow where candidate drugs (green) can bind the enzyme. Credit: Z. Jin *et al.*/*Nature*

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9 April — Absent antibodies suggest mystery immune response

After recovering from infection with SARS-Cov-2, many people have high levels of antibodies against the virus. But a recent study finds that in some recovered patients, such antibodies are present at very low levels — and in some cases are undetectable.

When a foreign microbe intrudes on the body, the immune system usually makes proteins called antibodies that help to fight off the invader. A team led by Jinghe Huang and Fan Wu at Fudan University in Shanghai, China measured antibodies to the novel coronavirus in 175 volunteers who had recovered from mild infections (F. Wu *et al*. https://www.medrxiv.org/content/10.1101/2020.03.30.20047365v1, 2020). About 30% of the volunteers — and especially those under the age of 40 — never developed high levels of SARS-CoV-2 antibodies, suggesting that other immune responses helped rid them of their infections.

8 April — Viral load soars as infected people start feeling ill

Viral RNA levels are highest in people with COVID-19 soon after their symptoms appear, according to two separate research teams.

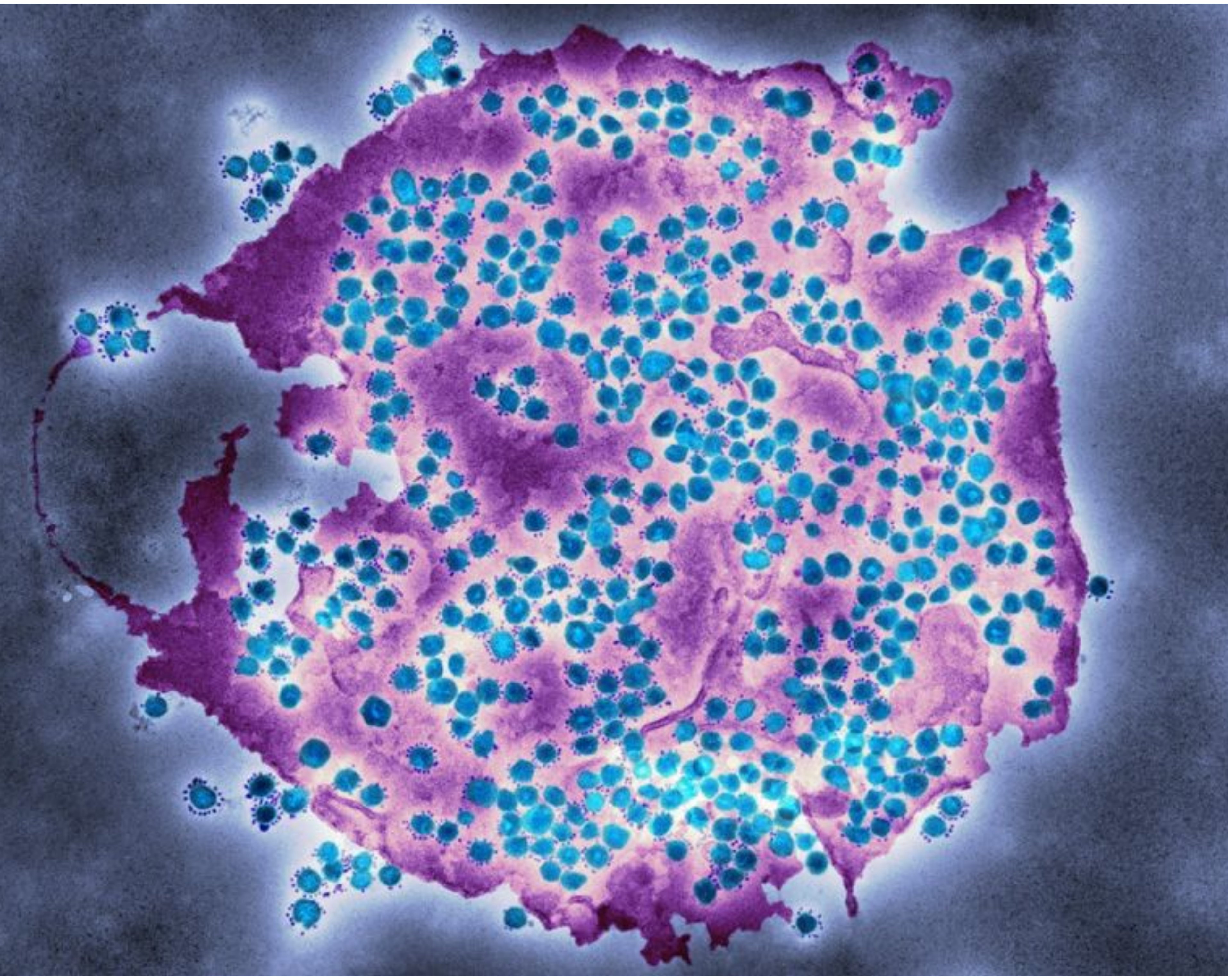
Kwok-Yung Yuen at The University of Hong Kong–Shenzhen Hospital, China, and his colleagues analysed saliva samples coughed up by 23 people infected with SARS-CoV-2. The team found that study participants' viral concentrations peaked shortly after they started feeling ill, and began declining about one week after the peak.

The more viral RNA detected in a person's body, the more they excrete when coughing or sneezing. The authors say that the high levels of SARS-CoV-2 particles detected at the onset of symptoms suggest that the virus can be transmitted easily between people, even when symptoms are relatively mild (K. K.-W. To *et al. Lancet Infect. Dis.* http://doi.org/ggp4qx; 2020).

The results are consistent with another study of nose and throat swabs from 18 people with COVID-19. The concentrations of viral RNA in the 17 symptomatic patients were similar to that in the one asymptomatic patient (L. Zou *et al. N. Engl. J. Med.* http://doi.org/ggmzsp; 2020).

However, another study found that people with milder COVID-19 symptoms on admission to hospital had much lower concentrations of viral RNA than did those with more severe symptoms (Y. Liu *et al. Lancet Infect. Dis.* http://doi.org/dqrr; 2020). Wei Zhang at The First

Affiliated Hospital of Nanchang University, China, Leo Poon at the University of Hong Kong, and their colleagues say the findings suggest that viral RNA concentrations could predict whether infected people will develop more severe symptoms.



Particles (blue) of the virus that causes COVID-19. Credit: NATIONAL INFECTION SERVICE/SPL

7 April — A comparison finds subtle differences between tests for the COVID-19 virus

Doctors rely on a test called quantitative reverse-transcription polymerase chain reaction (qRT-PCR) to determine whether a person is infected with SARS-CoV-2. A team led by Nathan Grubaugh at Yale School of Public Health in New Haven, Connecticut, compared nine widely used versions of the test and found that all of them reliably detect the virus (C. B. F. Vogels *et al*. Preprint at medRxiv https://www.medrxiv.org/content/10.1101/2020.03.30.20048108v1;

2020).

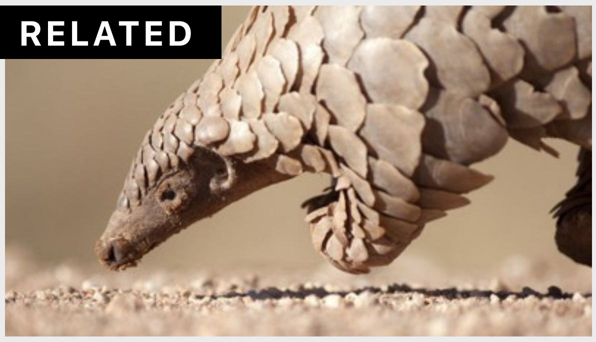
But the researchers also found that some tests — including one made by the US Centers for Disease Control and Prevention, another developed at Hong Kong University, and a third from Charité–Universitätsmedizin Berlin — performed best when it came to detecting low levels of the virus in samples.

5 April — Bats harbour a pool of coronaviruses related to pandemic culprit

Viruses closely related to SARS-CoV-2, the virus causing the COVID-19 pandemic, have been circulating in horseshoe bats, ready to jump to humans, for decades — and maybe even longer.

David Robertson at the University of Glasgow, UK, and his colleagues analysed the RNA of 68 coronaviruses, including SARS-CoV-2 and the virus that causes severe acute respiratory syndrome, or SARS (M. F. Boni *et al.* Preprint at bioRxiv https://doi.org/10.1101/2020.03.30.015008; 2020). This analysis shows that horseshoe bats (*Rhinolophus* spp.) host an expanding lineage of viruses that, like SARS-CoV-2, can infect humans. The team estimates that the ancestor of SARS-CoV-2 split 40 to 70 years ago from the closely related bat virus RaTG13. Though the two viruses are highly similar genetically, RaTG13 doesn't infect humans.

RELATED



Mystery deepens over animal source of coronavirus

The analysis also suggests that viruses in the lineage are ready to jump to humans directly from bats. But SARS-CoV-2 might have first hopped to another species that humans are more exposed to, rather than spreading straight from bat to human.

3 April — Masks could cut spread of COVID-19 virus

Surgical face masks effectively block the spread of seasonal coronaviruses in respiratory droplets, suggesting that masks could prevent transmission of SARS-CoV-2.

Seasonal coronaviruses are one cause of the common cold. Benjamin Cowling at the

University of Hong Kong and his colleagues had ill volunteers who were infected with seasonal coronaviruses sit in an enclosed booth and place their faces in a sampling device, called the Gesundheit-II, that captures airborne particles (N. H. L. Leung *et al. Nat. Med*. https://doi.org/10.1038/s41591-020-0843-2; 2020).

The scientists detected coronavirus RNA in both coarse droplets and finer 'aerosol' droplets emitted by volunteers who were not wearing masks. Mask reduced detection of viral RNA in both types of droplet. Larger particles are carried by sneezes and coughs, whereas exhaled breath can spread aerosol droplets, which have a diameter of five micrometres or less.

The authors say that surgical masks reduce transmission of not only seasonal coronaviruses, but also influenza.

Correction: An earlier version of this article said masks reduced detection of viral DNA.

1 April — Antibodies from llamas help to foil the COVID-19 virus

Antibodies from llamas (*Lama glama*) could help in the fight against several coronaviruses that infect humans.

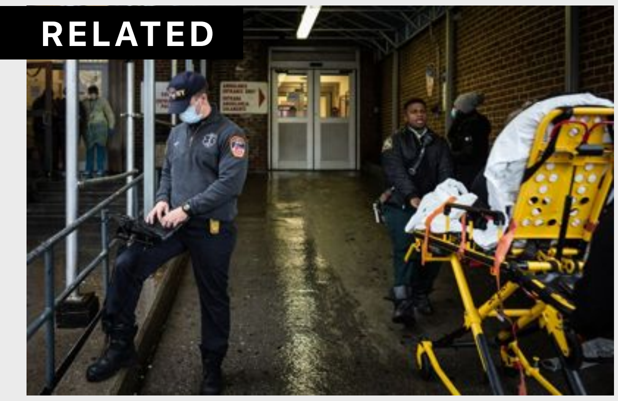
A team led by Bert Schepens and Xavier Saelens of the VIB life-sciences institute in Ghent, Belgium, and Jason McLellan of the University of Texas at Austin has isolated two llama antibodies that bind the 'spike' proteins that coronaviruses use to enter cells (D. Wrapp *et al*. Preprint at bioRxiv https://doi.org/10.1101/2020.03.26.010165; 2020). One antibody neutralized the coronavirus responsible for Middle East respiratory syndrome (MERS); the second mopped up the severe acute respiratory syndrome (SARS) coronavirus.

Fusing the SARS antibody from a llama with an antibody from a human yielded a hybrid that neutralized the virus responsible for COVID-19. The data suggest that such antibodies could be useful in combating coronavirus epidemics

30 March — Debilitated patients rally after dose of survivors' blood

People seriously ill with COVID-19 experienced striking improvement after receiving infusions of blood from disease survivors, according to two separate research teams.

Both teams extracted antibody-laden plasma — a component of blood — from people who'd recovered from COVID-19.



How blood from coronavirus survivors might save lives

Xiaoming Yang at the National Engineering Technology Research Center for Combined Vaccines in Wuhan, China, and his colleagues gave the plasma to ten severely ill people. By the sixth day after the treatment, the virus that causes COVID-19 was undetectable in seven of the ten. The recipients experienced no significant side effects (K. Duan *et al*. Preprint at medRxiv http://doi.org/dqrs; 2020).

A group led by Lei Liu at Shenzhen Third People's Hospital in China gave survivors' plasma to five "critically ill" people (C. Shen *et al. J. Am. Med. Assoc*. http://doi.org/dqn7; 2020). Symptoms dwindled in all five; within ten days of receiving the plasma, three recipients no longer needed ventilators.

Other researchers would like to try such transfusions to treat health workers who have been directly exposed.

27 March — Viral proteins point to potential treatments

A list of the human proteins affected by the SARS-CoV-2 virus offers a guide to potential treatments for infected people.

A team led by Nevan Krogan at the University of California, San Francisco, engineered human cells to produce one of 26 proteins made by the coronavirus (D. E. Gordon *et al.* Preprint at bioRxiv https://doi.org/10.1101/2020.03.22.002386; 2020). This allowed the researchers to identify human proteins that physically interact with coronavirus proteins.

Out of 332 interactions between human and viral proteins, the authors identified 67 that existing or candidate drugs could potentially disrupt. The researchers and their collaborators are now testing some of these compounds for antiviral activity — and urge others to do the same.

doi: 10.1038/d41586-020-00502-w

Nature ISSN 1476-4687 (online)