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Covid-19

Fail unsafe

Better surveillance, not restrictions on travel, is the way to deal with dangerous covid variants, old and new

JANUARY 5TH was the third anniversary of the day that researchers at the Wuhan Institute of Virology, in China, isolated a coronavirus which had caused a cluster of mysterious pneumonia cases in one of the city's hospitals. This new virus, named SARS-COV-2 by the World Health Organisation (WHO), has subsequently infected most of the world's population. In parts of Europe the percentage of people who have never caught it is probably in single digits.

Vaccines and prior infections have now slowed SARS-COV-2's spread. But it has evolved partial means to evade the immunity they confer. Reinfections have become routine. In light of this, attention has turned once more to China. The country in which covid started has only recently followed the rest of the world by abandoning isolation and lockdowns (see China section). That, combined with its patchy record on vaccination—meaning many Chinese have had no opportunity to acquire immunity from either an infection or a vaccine—has resulted in a surge of cases. And the outside world has responded.

Many countries have increased their testing of arrivals from China. America, Britain, France and Italy, in particular, now require travellers from Chinese airports to produce evidence of a negative covid test. And America, which already gathers swabs anonymously and voluntarily from people arriving from more than 30 countries, in order to monitor variants circulating overseas, is expanding the number of flights per week covered by the programme to 500, including 290 from China.

Most experts question the value of preflight testing. The variants dominant in China are already circulating through the populations of countries requiring it, so Chinese arrivals, these experts reckon, will make little difference. But monitoring is a different matter. That is sensible. One underlying fear is that the end of China's lockdown means a new, resurgent, variant of the virus may evolve and emerge from co-

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vid's original homeland. Such fears are not assuaged by the fact that China, though still reporting genomic-sequencing data, no longer publishes numbers of cases, hospital admissions or deaths.

But other countries, too, are doing less than they used to in the matter of monitoring. According to Maria Van Kerkhove of the WHO, the number of SARS-CoV-2 sequences submitted to GISAID, an international repository of viral genetic information, has dropped by 90% since the start of 2022, and the number of countries submitting data has also fallen. Official attitudes have, she says, become complacent. The thinking has been that the illness is now milder, that there is nothing more to do and that (events in China notwithstanding) the pandemic is over. But it isn't. Covid still kills 10,000 people a week, and many of those deaths are preventable.

Network theory

Following the evolution of SARS-CoV-2 is the task of networks of laboratories that sequence the genetic makeup of viral samples circulating around the world. When the virus breeds in an infected individual the offspring are not always exact replicas of those from which they are spawned. Spelling mistakes in the genetic code occur routinely during replication. Most of the results are cosmetic, changing a virus's look, but not how it functions. Occasionally, though, alterations occur that dictate how easily it infects human cells, or which types of cell (upper- or lower-respiratory-tract cells, for example) are most susceptible. With many such changes, a virus may become better at spreading, at making people ill, or both.

If a variant with unusually many mutations is spotted, epidemiologists chime in. They investigate whether places where this particular variant is on the rise are also seeing a faster spread of infections, cases that are more severe, or evidence that covid tests, drugs and vaccines are less effective than elsewhere. If this information suggests existing measures are failing, the new virus is designated a variant of concern (VOC) by the WHO, and is given a name from the Greek alphabet.

Each new VOC has been more transmissible than its predecessors. Delta was, on top of that, more severe. Omicron, the latest, is less severe than Delta. But a future variant might swing the other way again. "There is this notion that the more this virus circulates, the less severe it will become. There is absolutely no guarantee of that," says Dr Van Kerkhove.

Since Omicron emerged in late 2021, no new VOC has been designated. New lineages have evolved, each better than its predecessor at evading immunity—but these do not, in the WHO's view, merit radical changes in public-health measures. They have thus not been upgraded to VOCs and instead go by alphanumeric codes, such as "XBB.1.5" for the form of Omicron now becoming dominant in America.

The importance of lineage

Nobody knows exactly how fitter lineages of SARS-CoV-2 emerge. One hypothesis is that they originate in people with suppressed immune systems, such as those with cancer or HIV/AIDS, or who are taking drugs to prevent the rejection of transplanted organs. Individuals like these can remain infected with SARS-CoV-2 for months, giving the virus lots of time to accumulate mutations as it replicates.

Research on people with compromised immune systems has indeed found that the SARS-CoV-2 variants in their bodies have unusually large numbers of mutations. But a study of 27 such patients, published in June 2022 in *Nature Medicine*, showed that the variants they carried were missing important mutations, common in VOCs, which are related to better transmission. Nor did these patients transmit the virus to others (though that could be because many were bedridden, and some had isolated themselves). This study suggests that variants which arise in such patients are better at replicating in those patients' bodies, but no better at transmitting themselves to others.

Another theory about how VOCs originate is back-and-forth transmission of SARS-CoV-2 between people and other animals. Transmission from humans to cats, dogs, mink and deer has been documented. Some research has found that viral mutations in animals infected by human-derived SARS-CoV-2 are in parts of the genome that are changed in VOCs, such as that encoding the spike protein which the

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virus uses to latch onto cells.

For a VOC to arise in this way, a variant transmitted from an animal to a human must be able to spread subsequently from person to person. This did not happen in a cluster of mink-to-human SARS-COV-2 transmissions at a fur farm in Denmark in 2020. The mink virus that infected people looked scary because it was heavily mutated in the animals. But people who caught it did not pass it to others. Still, such transmissions remain a concern. Flu viruses also cross back and forth between animals and people. And though animal flu viruses that infect humans usually go no further, there are exceptions, such as the 2009-10 flu pandemic, which was caused by a virus that probably came from pigs.

Another worry at this stage of the pandemic is the possibility of recombinant viruses. These happen when someone is infected with two variants simultaneously. This allows the pair to swap genetic material, resulting in offspring that carry mutations from both. That permits particularly troublesome combinations. XBB.1.5, for example, evolved from a fusion of two Omicron lineages. The original XBB lineage was good at dodging antibodies but poor at latching onto human cells (which determines infectivity). XBB.1.5 is good at both.

If a consensus exists on one thing about VOCs, says David Heymann of the London School of Hygiene and Tropical Medicine, it is that they emerge at random, and may do so anywhere at any time. No evidence is known that variants are more likely to arise in populations with less immunity, such as China's. More infections do mean a greater chance of such a random event happening, which is why China's sudden unlocking, and the surge of cases that has accompanied it, is worrisome. But the additional risk is different only in degree, not in kind, from that which already exists in the rest of the world.

Regardless of any Chinese contribution, though, periodic covid waves are here to stay. That is because none of the covid-19 vaccines so far available is good at preventing infections for more than a short period after administration. Dealing with SARS-COV-2 variants is therefore less a matter of stopping transmission than of constant monitoring and adjusting covid tests, treatments and vaccines as needed.

Data, data, data

And it is this monitoring which is getting harder. The WHO's covid-surveillance system relies on genomic-sequence data submitted from laboratories around the world to organisations such as GISAID, to show which variants are becoming dominant in various parts of the planet, whether those variants are more virulent, and how successful drugs and vaccines are against them. No sequences means no information on these points. Similarly, the WHO also tracks the proportion of cases caused by new variants that require admission to hospital, and, once there, transfer from normal wards to intensive care. That helps gauge changes in severity. But the means to collect these data, too, are disappearing, according to Dr Van Kerkhove.

There is a deeper problem, as well. Dismantling the testing, sequencing and surveillance capacity built up in the past three years risks leaving the world unprepared for the next pandemic. Hopes that politicians might, at last, see pandemic illness in the way that they see the defence of the realm, as something requiring the maintenance of a permanent establishment ready to counter threats, seem to be fading.

In this respect alone, China's botched unlocking, though terrible for the people of that country, may have a silver lining. If it causes a rethink elsewhere about the importance of monitoring for the long term, that will be a global good. ■

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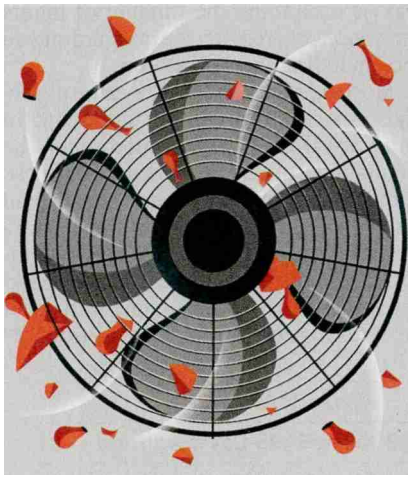
Acid drops

A way to purge air of the virus that causes covid-19

IN CHINA, ONE sign a respiratory disease is doing the rounds is a rise in sales of vinegar. Folk medicine says that when you boil it, the acetic-acid-rich fumes clear the air of whatever nastiness is bringing on the cough. And there may be a grain of truth in this belief, for one sure way to render airborne viruses, such as SARS-CoV-2, the cause of covid-19, harmless, is to make the droplets of fluid which carry them more acidic.

Tamar Kohn of the Swiss Federal Institute of Technology in Lausanne, and Thomas Peter of its Zurich counterpart, reckon, though, that this can be done well only by a stronger acid than acetic—nitric, for example. They observe in a study just published in *Environmental Science and Technology* that once inside a droplet, nitric acid creates conditions which viruses find really hard to take.

Dr Kohn, Dr Peter and their collaborators experimented with various viruses suspended in liquids of the kinds that natural virus-carrying aerosols are made of—lung fluid and nasal mucus in particular—to see how acidic these would have to be to inactivate different viral species. Based on previous experiments on the diffusion of compounds into such droplets, they also calculated how easily nitric acid would enter them.



The logical next step would have been to study the effect on aerosol-borne viruses of air rich in nitric acid. They were, however, prevented from doing this by biosafety regulations, so instead they used a computer model based on the results they had collected.

For influenza viruses, the model suggested, normal room air is already quite harmful. Flu bugs are inactivated by it in minutes. SARS-CoV-2, however, is a harder nut to crack. In normal room air it can remain active for days. But invulnerable it is not. Droplets become death traps for it in under a minute if the acidity of the air is increased sufficiently. And that suggests an intriguing idea. Injecting nitric acid into a building's air, via its ventilation system, might, the model indicates, reduce the chance of infection for people 1,000-fold.

That would involve people breathing in strong acid. But this should not be harmful. The concentration required to destroy SARS-CoV-2 is less than a tenth of the legal safe level for workplaces in America and much of Europe.

Whether, even with that reassurance, people would actually be willing to accept acidic air in exchange for viral protection remains to be seen. But one clear consequence of this work is that it is worth considering wearing a mask in buildings such as museums and libraries which are filled with things that acid is bad for, and thus have their air treated to reduce, rather than increase, its acidity.