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Down To Earth

FORTNIGHTLY ON POLITICS OF DEVELOPMENT, ENVIRONMENT AND HEALTH

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COVID-19

TESTING ON TRIAL

Widespread and varied testing alone cannot help overcome the pandemic. A robust health infrastructure holds the key

MIGRATORY DILEMMAS

Around 100 million informal workers in India have returned to their villages due to job loss because of the lockdown. But the government's revival package has offered them only more debt

AS THE monsoon clouds enveloped Kerala, thousands of workers from across India were migrating to their villages. Even though they had been surviving on daily wages, May is the month they would normally return to their original—and seasonal— source of livelihood: farming. But this year the seasonal migration back to village was not about a romantic notion of people still rooted in their ancestral occupation—there was no aura of a homecoming with hopes and the joys of producing critical foodgrains for a few months, and, there was no eagerness to reach home and inform their families on a big saving to be invested in many essentials, including on farms. On the contrary, India's monsoon season has begun with a deluge of woes—for workers, farmers and farming. And this is going to be the most devastating spillover of the COVID-19 pandemic.

Amid the lockdown—India's 68 days is the longest in the world—the country not only reported a consistent rise in COVID-19 cases, it also willingly reconciled to live with the virus (see infographic 'Newer targets' on *p*37). By May 31, when most of the restrictions were lifted, the enormity of the pandemic simply shrunk into oblivion, masking another crisis of a much bigger scale.

FORCED MIGRATION

For the past two months, millions of workers were forced to return to their villages. But this was not

PHOTOGRAPH: REUTERS

the usual monsoon reverse migration; they were left unemployed due to the cessation of economic activities in cities and towns. “It seemed there were more people on the roads than in villages,” says Vivek Mishra, a correspondent with *Down To Earth* who has been walking with migrants to track and chronicle this unfolding economic mayhem. Their “forced” migration made the pandemic look insignificant, in terms of human suffering. Headlines changed: pandemic as a prefix to this crisis was succinctly replaced with the economic crisis.

Ekta Parishad, a non-profit helping migrant workers return home across India, has collected primary information of 31,424 migrants between April 11 and May 20. Of the 24,681 stranded adults, 37 per cent were daily-wage earners, followed by industrial labourers such as construction workers (30 per cent), farm labourers (26 per cent), and labourers employed in the service sector (7 per cent).

It is estimated that 100 million workers have moved away from urban areas in these two months. That would make it the biggest-ever movement of people in India’s history. But it is also the most disruptive economic development. India’s villages were already economically wrecked, forcing people to migrate to towns and cities for livelihood. Now, with millions returning to the villages, an urgent expansion of the rural economy is required to sustain this transition.

To begin with, each of these workers has a family to sustain. Together, these informal workers contribute around 10 per cent to India’s GDP. Add to it the fact that the agriculture sector’s contribution to GDP is 15-16 per cent; which also primarily comes from these workers. Put together, they decide the economic fate of the country.

The challenge now is how to reinvent an economy of such scale immediately to sustain the homecoming workers. The great migration is happening at a time when, in fact, policymakers were expecting migration out of rural areas, given the economic situation existing there. For instance, since January unseasonal rains and extreme weather events damaged the winter cash crops. Due to a low demand in the markets, farmers were not even earning a fair price for their produce, thus taking a further cut in their meagre earnings.

DISPLACED PEOPLE, MISPLACED MINDSET

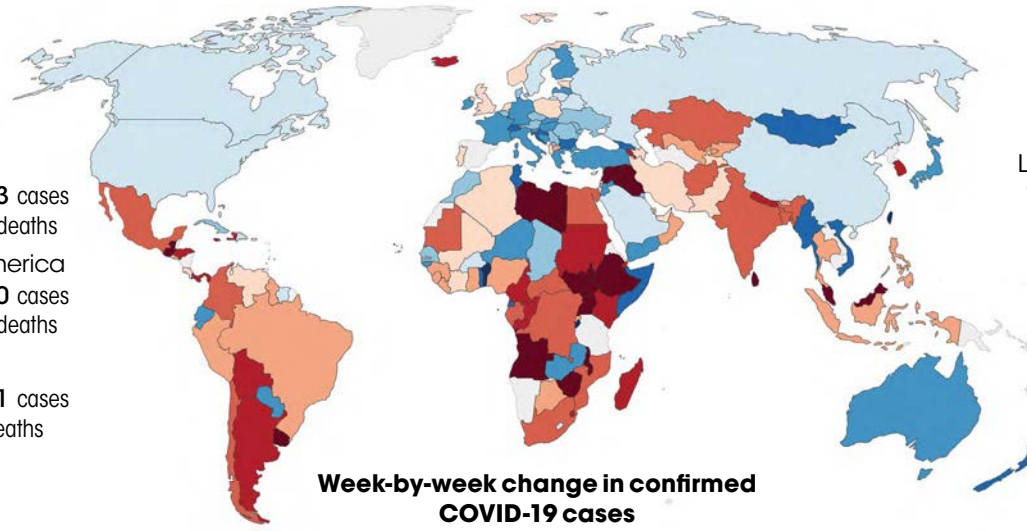
Internal displacements because of disasters like cyclones and floods are common in India. There were more than 5 million new displacements in 2019—the most in the world—according to Geneva-based Internal Displacement Monitoring Centre (IDMC). And the bulk of the displacements were triggered by extreme weather events that are linked to climate change. In terms of scale, India saw the wettest monsoon in 25 years in 2019, which triggered 2.6 million new displacements. Cyclone Fani was responsible for another 1.8 million new displacements in the same year. Similar numbers are expected this year too due to Cyclone Amphan and the near definite signs of a weak monsoon.

However, the lockdown—coinciding with the harvesting season for

Europe
1,986,063 cases
172,457 deaths

North America
1,994,770 cases
121,233 deaths

Asia
1,079,861 cases
29,653 deaths



Latin America
766,534 cases
36,937 deaths

Africa
133,196 cases
3,871 deaths

Oceania
8,782 cases
125 deaths

Figures till May 28, 2020

Week-by-week change in confirmed COVID-19 cases

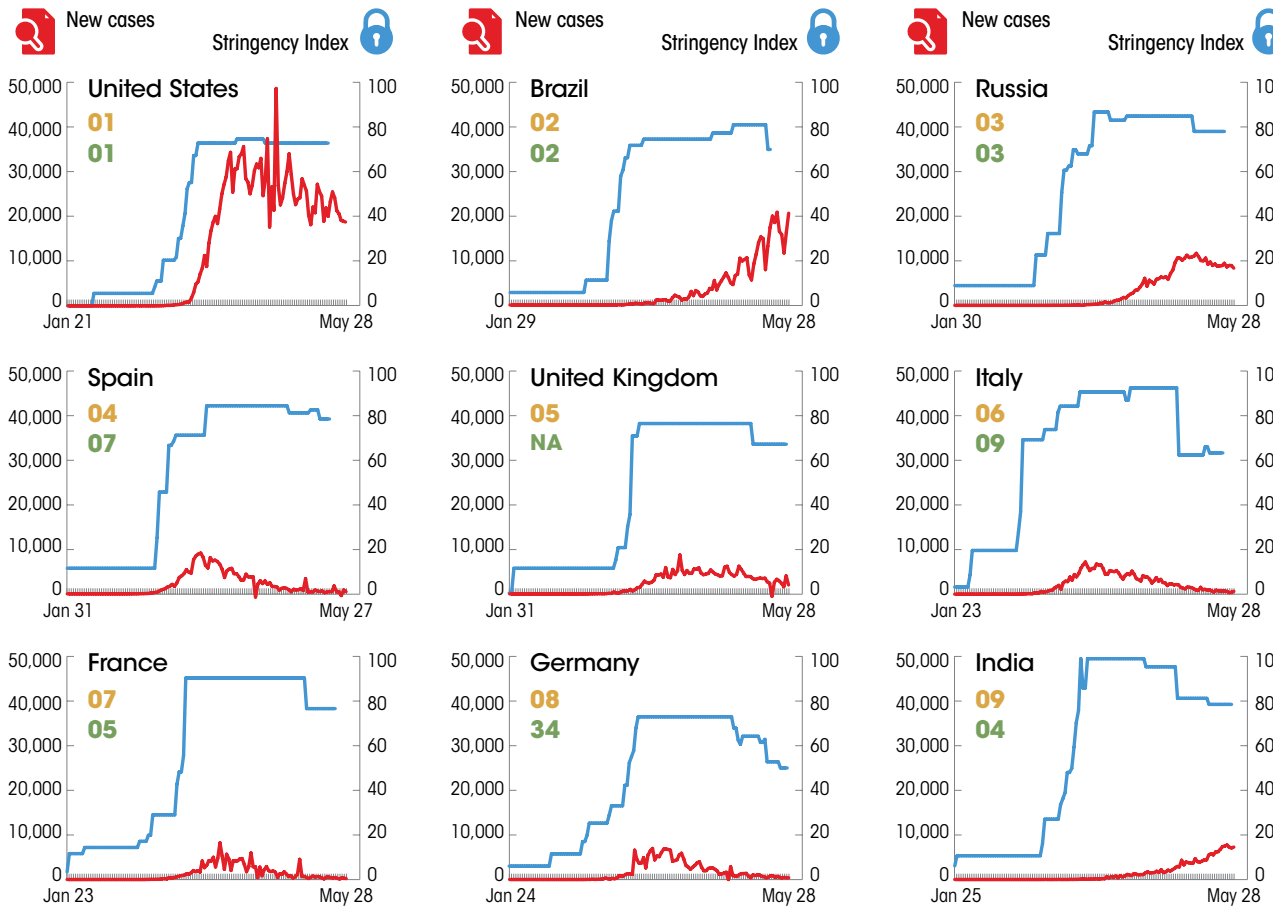
No data | <-500% | -100% | -50% | 0% | 10% | 25% | 50% | 100% | >500%

% change in the number of new confirmed cases between May 15-21 and May 22-28, 2020

NEWER TARGETS

While new cases remain static or are on a downhill in North America, Europe and Australia, countries in Latin America, Africa and certain parts of Asia are emerging as the new hotspots

India and Brazil are two of the nine worst-hit countries. Governments are easing stringency measures even as new cases continue to mount. India ranks 4th globally in terms of active cases; Brazil 2nd



00 Rank (total cases); **00** Rank (active cases)

Source: European Centre for Disease Prevention and Control

GRAPHIC: SANJIT / CSE

PHOTOGRAPH: REUTERS

winter crops—means that the farmers are losing a significant chunk of their earnings. More than half the farmers who harvested their crops this year suffered a lower yield during the nationwide lockdown, compared to the last season of sowing the same crop, says the survey of 1,500 farmers in 200 districts across 12 states. The lockdown also forced 55 per cent of farmers to store their crops as they were unable to sell them.

The IDMC survey—aimed to evaluate the impact of lockdown on agricultural production and livelihood—was conducted by the Harvard TH Chan School of Public Health, Public Health Foundation of India and the Centre for Sustainable Agriculture from May 3 to May 15, 2020. Farmers in Andhra Pradesh, Bihar, Gujarat, Haryana, Karnataka, Madhya Pradesh, Maharashtra, Punjab, Rajasthan,

PREVIOUS EDITIONS ON COVID-19
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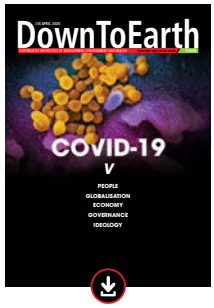

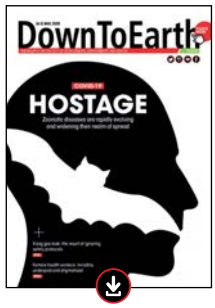

Telangana, Uttar Pradesh and West Bengal participated in the survey. About 40 per cent of farmers who experienced a yield loss say this was due to lack of labour, storage or transport options. Unexpected weather change was also cited as a reason for the loss in yield by 80 per cent of farmers, found the survey.

"We call this the Great Lockdown, because, if you look around the world, the containment measures that have been put in place...are generating the scale of contraction and activity that are just historical numbers," says Gita Gopinath, chief economist of IMF in a podcast. On May 22, the Governor of Reserve Bank of India Shaktikanta Das declared the Indian economy would shrink, for the first time in 41 years, or there would be negative growth. The top six industrialised states in India, which account about 60 of industrial output, are severely impacted by the COVID-19 lockdown. These are the states that have reported the maximum outflow of workers. This means that employment generation would be very difficult in these states in the near future.

RELIEF: NOT RUPEES, BUT LOANS

The Union government announced a ₹20 lakh crore economic stimulus package, which the government has claimed will provide relief to migrant workers, farmers and other sections of society that suffered from the nationwide lockdown. The package, however, seems to consist more of loan offerings, rather than a comprehensive stimulus. When Finance Minister Nirmala Sitharaman explained the details in press conferences—stretching over five days—the announcements seemed more of a loan offering, with calls to privatise national assets.

Everything the government offered was a loan, except for the decision to give free ration to poor families and a meagre amount of ₹500-₹1,000 for Jan Dhan account holders, widows, the elderly and the differently abled. If one were to interpret the government's version, people have to first take loans, invest in businesses, and, then wait for results to get relief—something that may take years to come.

The finance minister also announced a credit programme for street vendors as well, where they can take loans of ₹10,000. But it is unclear as to who will be chosen for the programme. Is there a database of street vendors and what documents they will need? The same is the case for farmers, where Sitharaman relied too much on Kisan Credit Cards, despite the fact that only 40 per cent of India's small and marginal farmers are covered by formal credit, as of 2019, according to the Reserve Bank of India. The economic package may have stolen the attention from the pandemic itself, but the economic infection is only now going to unfold. DTE

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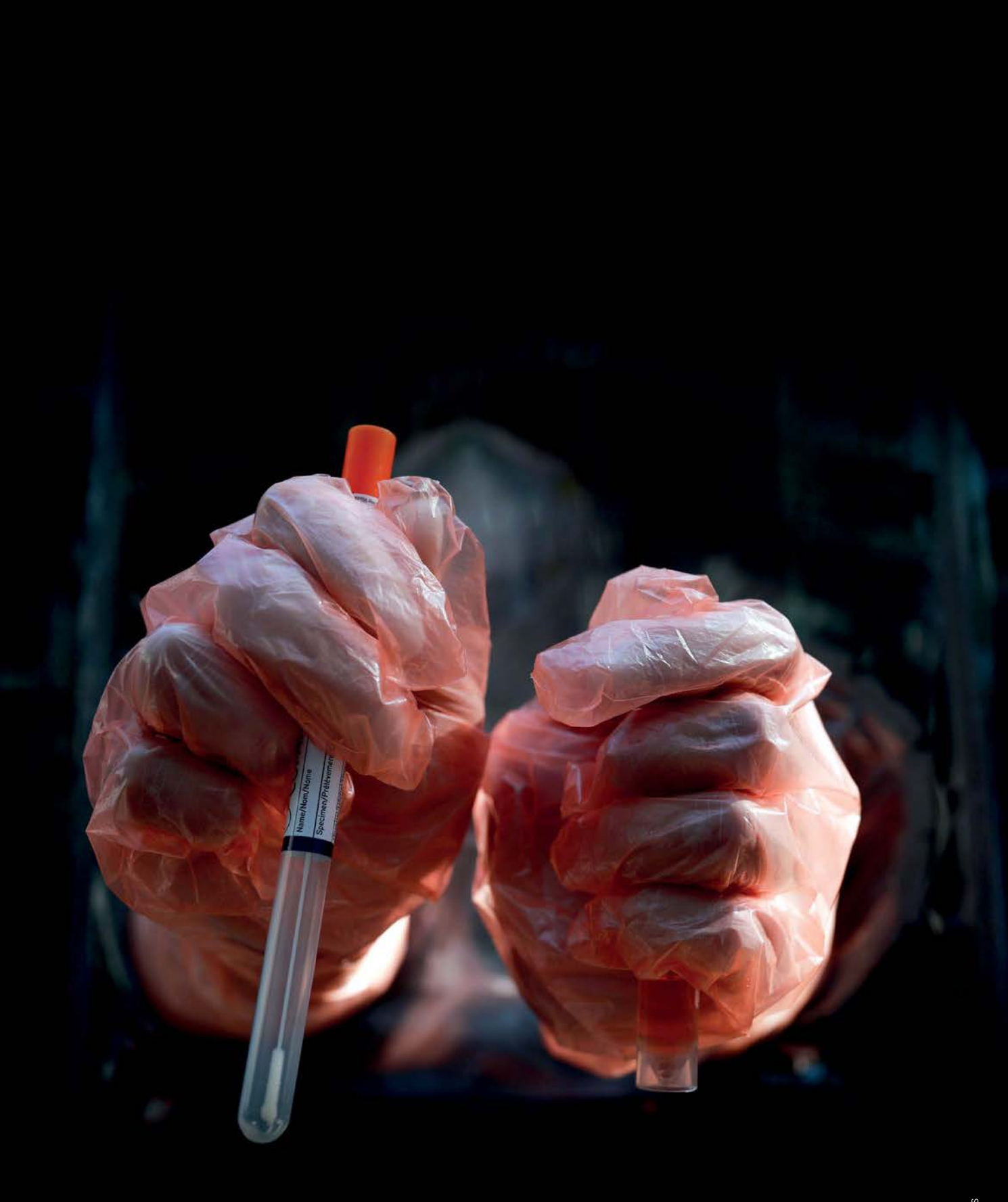


PHOTO: REUTERS

SAMPLE THE UNKOWN

Testing is no doubt the cornerstone of the fight against COVID-19. But the world's growing obsession with tests might weaken our response to the pandemic.

VIBHA VARSHNEY explains

THE WORLD is in a rush to reopen. After some five months of closure due to the COVID-19 pandemic and amid the forecast of a 3 per cent drop in the global economy—the steepest since the Great Depression of the 1930s—governments are easing stay-at-home orders, lifting restrictions and even drafting new laws to make up for the lost days. But with no antidote or vaccine in sight, they are in a fix; any careless move can undermine the hard-fought gains and lead to an explosion of new cases. In India, where the Union government has been relaxing restrictions while extending the lockdown, states are nervous as the infection count continues to rise. But as Australia's Prime Minister Scott Morrison says about easing lockdown: "It's going to be step by step, there is going to be some trial and error, this is completely uncharted territory."

The world is frantically looking for role models—countries that have weathered the pandemic storm and have worked out plans to reanimate their economies. One country that has emerged as a sign of hope is South Korea. Rising like a phoenix from the ashes, it has come out stronger from a similar crisis in 2015 when an outbreak of the highly-fatal Middle East Respiratory Syndrome (MERS), also caused by a coronavirus, sickened 186 people and killed 38. So on January 20 this year, when the country reported its first COVID-19 case, health officials knew they had to quickly quarantine the infected and trace those who came in contact with them before they could spread the disease further. Its biotech industry had, in fact, started working on a diagnostic kit much earlier, as soon as China, the country of origin of the disease, released the genome of the virus, SARS-COV-2. By February 12, when the total number of cases were way below 100, the Korea Centers for Disease Control and Prevention had approved the test kit by one local biotech company, Seegene, on a fast track basis. Such approvals typically take a minimum of six months. Soon, other companies joined forces.

With the diagnostic kits in hand, the country launched a massive testing and contact-tracing campaign. Even asymptomatic people could get themselves tested for free. Since hospitals had turned into hotbeds of infection during the MERS outbreak—paralysing the healthcare delivery system—this time the

^ A drive-through testing facility in South Korea. Using its experience from the MERS outbreak in 2015, the country has not only set up a huge infrastructure for testing but also kept them separate from treatment facilities to avoid the spread of infection

PHOTO: REUTERS

country kept the testing and treatment facilities separate. By early April, it flattened the curve and held the parliamentary election. It now has a huge infrastructure for COVID-19 diagnosis—638 testing centres, including 80 drive-through screening kiosks, and a capacity to test 23,000 people a day. It did not have to resort to lockdowns. The International Monetary Fund (IMF) says the country's GDP would shrink only by 1.2 per cent this year.

Small wonder, widespread testing has become the mantra for defeating COVID-19. In the US, as President Donald Trump wants Americans to return to work and get the economy running, state governors are pushing and fighting for more tests. In the third week of May when the death toll neared the 100,000 mark—the highest in the world—the White House rebuked its top health agency, the Centers for Disease Control and Prevention (CDC), saying "it let the country down" on providing testing. CDC had botched up the testing kit it was asked to develop. It was only on February 28, a month after the first case was reported in the country, that CDC decided to rope in other public and private entities for developing tests. By April 27, the Food and Drug Administration (FDA) had issued emergency-use authorisation to 70 test developers. That day, Trump unveiled two documents—*Testing Overview* and *Testing Blueprint*—and said a big part of "opening up America again" depends on testing to determine how many had been exposed to the virus. By May 21, it was conducting 39.42 tests per 1,000 people; South Korea's testing rate is 15.65 per 1,000.

In Africa, authorities are meanwhile struggling to compete with richer countries for procuring testing material on the global market. Even where there is enough money, many African health authorities are unable to obtain the supplies needed, says a commentary published published in

The Lancet scientific journal on May 7.

There's no doubt that testing is the cornerstone of this fight against COVID-19. But it seems more than helping in the combat, it has led to confusion and chaos worldwide. Can governments rely on them for reopening economies?

Here's an uneasy answer

First, let's delve into the world of diagnostic tests where every reaction and every chemical matters

Broadly, two methods of tests are available for SARS-CoV-2: molecular, which looks for the presence of the virus or its genetic material in the sample of nasal mucous or saliva, and serological, which looks for the presence of antibodies in the blood.

The first one is based on a routine lab technique, reverse transcription polymerase chain reaction (RT-PCR), which amplifies the minuscule amount genetic material in a pathogen and helps identify it. The technique has to be customised as per the disease by using primers, or short nucleic acid sequences, specific to the pathogen's genetic material. Typically, the procedure involves sticking a swab, similar to an earbud, but uses nylon instead of cotton, deep into the nose or throat, retrieving mucous sample, placing the swab in buffer solution to transport and isolate the virus, replicating its genetic material using chemicals or reagents like primers, enzymes and nucleotides, and then detecting it with fluorescent probes. Once the sample reaches lab, the entire process takes six hours (see 'Not so easy hunt', *p*47).

The serological test kit, on the other hand, is simpler and portable, just like a pregnancy test kit, and can give results in 20-30 minutes. It is also cheaper—in India, a rapid antibody test costs about ₹400 compared to RT-PCR that costs ₹4,500. Based on a drop of blood, these test strips look for antibodies that are produced as a natural defence mechanism of the body when exposed to a pathogen. Thus, it not only helps find out those who were infected and subsequently recovered, it also helps identify asymptomatic patients who could have silently spread the infection.

BOTH THE TESTS HAVE LIMITATIONS. FOR ONE, NONE OF THEM CAN TELL FOR SURE IF A PERSON IS COVID-19-POSITIVE OR NEGATIVE. THESE FLAWS ARE NOW MORE PRONOUNCED BECAUSE OF THE HASTE WITH WHICH THE TESTING MACHINES AND KITS ARE BEING DEVELOPED, REVIWED AND APPROVED

But the effectiveness of any medical test depends on accurate diagnosis. This is assessed in two ways: specificity and sensitivity. Sensitivity is the ability of a test to correctly identify those with the disease (true positive), whereas specificity is the ability of the test to identify those without the disease (true negative). This is crucial as the disease would continue to spread if a positive patient is reported negative. If someone tests false positive, then he or she would have to go through needless treatment and duress. Both the tests are mired in these specificity and sensitivity issues. This limitation is now getting more pronounced because of the haste with which the testing tools and kits are being developed and approved. Besides, never before has the world seen such a huge demand for tests. This has overwhelmed developers as well as suppliers, triggering shortages everywhere.

Let's examine RT-PCR

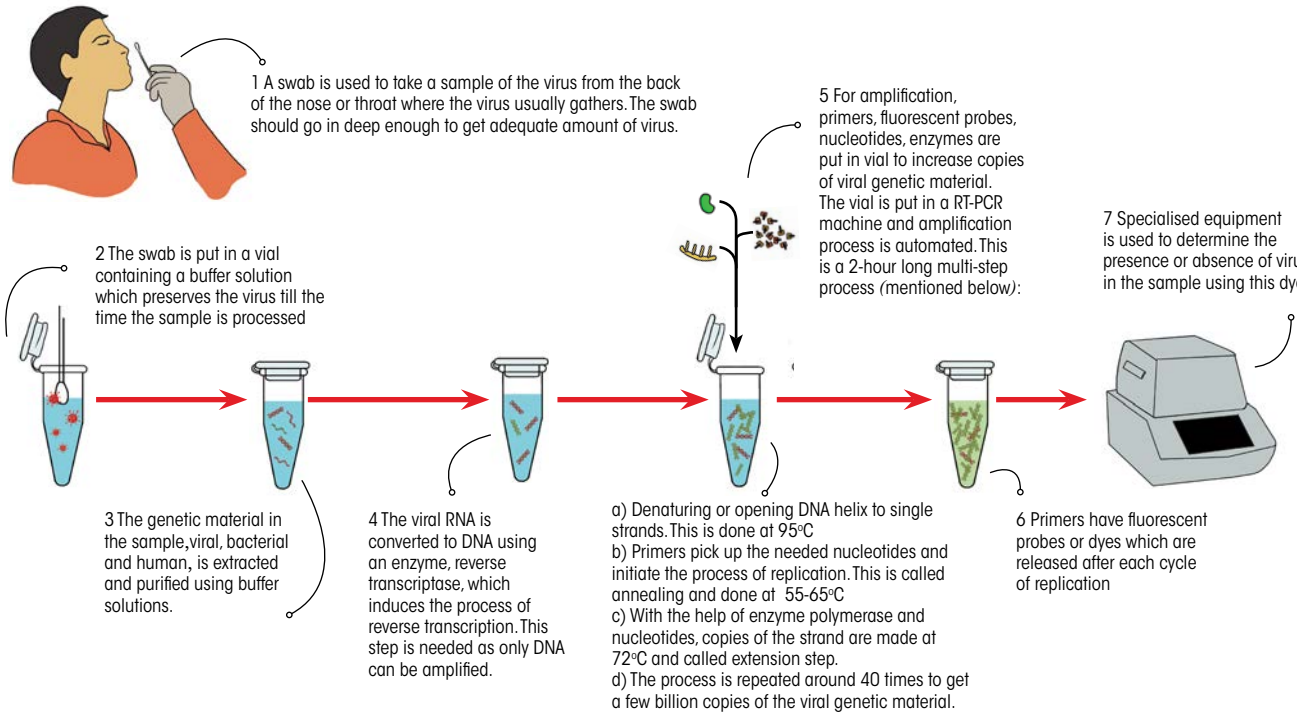
This test, considered the gold standard for COVID-19 diagnosis, depends on a robust supply chain for each and every ingredient. That's its major drawback

Between February and April, as active cases kept mounting, the world faced a shortage of COVID-19 RT-PCR testing kit components, right from swabs and buffer to enzymes. In the US, Colorado received 7 per cent of the swabs it had requested from the federal government till April 24. California received 90,000 of the 350,000 swabs it had asked for. To maximise the available swabs, CDC revised its guidelines on March 9 and asked technicians to collect one specimen swab instead of two.

A major problem with RT-PCR tests is that it depends on proprietary ingredients, protected by a registered trade name. These canot be quickly developed by other manufacturers to meet the shortfall. Although other versions of the ingredients might work, it's not easy to simply switch to a different type as even tiny changes

NOT SO EASY HUNT

RT-PCR technique is a gold standard test for infectious diseases. It is in high demand for diagnosis of COVID-19



can make the test fail. False results can be disastrous in this fight against COVID-19. In March-end, the Netherlands faced shortage in reagents. It asked Roche, which supplies to most Dutch labs, to share the recipe for its buffer solution. Under pressure from the European Commission, Roche agreed but shared a generic recipe available in text books. That month US also saw short supply of extraction reagent developed by Dutch company Qiagen.

"We will never have enough testing as reliance is on proprietary reagents. There needs to be more sources of PCR reagent, including from domestic producers," says Leena Menghaney, lawyer with humanitarian group Médecins Sans Frontières.

To overcome the shortage, researchers have come up with alternatives. One US-based Formlabs is working on 3D printing with pliable resin, which can replace the nylon swabs. Others are working on testing methodologies that simply would not require swabs. To reduce the dependence on buffer solution, dry swabs are also being developed. Some have found that a saline solution or standard buffer solution work equally well as the specialised ones. But these need to be validated by regulatory agencies before they are put to use. Any glitch can further reduce the reliability of RT-PCR, already fraught with accuracy issues. An analysis of the available RT-PCR kits for COVID-19 shows some have sensitivity of just 90 per cent and specificity of 96 per cent. In real world conditions, this could be just 66 to 80 per cent, which means one in every three would be falsely tested as negative.

Pitfalls mar antibody test too

It is portable, faster and cost-effective. But it isn't a diagnostic tool and can, at best, be used for research

The reason for this is simple. Our body develops antibodies only after a week or 10 days of being infected by a pathogen. Since rapid antibody test works by sensing these antibodies, it often fails to diagnose active cases. In a study posted on preprint server

Fighting blindfolded?

As countries focus on widespread testing, there seems to be little correlation between tests, disease burden and prevention of deaths

	Total tests/million population	Total cases/ million	Total deaths/ million
UAE	213,622	1,572	12
Russia	70,693	38,442	442
UK	59,593	6,707	944
Australia	56,080	503	7
New Zealand	55,751	539	8
USA	51,165	10,671	622
Canada	42,332	5,601	437
Venezuela	33,819	142	1
Peru	29,263	15,388	439
South Africa	11,482	4,299	90
Ghana	6,824	3,656	16
India	2,619	4,828	138

0-40,000	0-4,000	0-400
40,001-80,000	4,001-8,000	401-800
80,001 and above	8,001 and above	801 and above

Source: https://www.worldometers.info/coronavirus/; Data as on May 30, 2020

Methodology: *Down To Earth* selected from each continent two countries conducting maximum number of tests and compared their test rates (tests per million population) with the rates of cases (per million) and deaths (per million) in those countries. The countries have been ranked using a simple scale created on the basis of the rate values. For example, the US carried out low number of tests but had high number of cases and moderate number of deaths

medRxiv on April 20, researchers from the Oxford University, analysed nine COVID-19 rapid tests used in UK. Their specificity was good, between 85 and 100 per cent, but sensitivity was low, between 55 and 85 per cent. Due to low sensitivity, a positive result would indicate that the person was infected and has antibodies against the virus. But in case of a negative result, it is difficult to rule out if the person is infected. Thus, the researchers say, these tests are good for population-level surveys, but inadequate for patient applications.

The unreliability of antibody tests have been long known. In the case of influenza, its sensitivity is as low as 70 to 75 per cent, and thus false negative results are a major concern. Tests for dengue have variable performance, depending on the developer, serotype, medical history and duration of sickness. Even pregnancy kits that have been in use since 1976 and are generally considered reliable, have not been validated for reliability.

So when the World Health Organization (WHO) asked countries to "test, test, test", it talked only about RT-PCR. But a dipstick analysis shows that there is little correlation between widespread use of these tests, disease prevalence and prevention of deaths (see 'Fighting blindfolded?').

Down To Earth selected from each continent two countries conducting maximum number of tests and compared their test rates with their rates of cases and deaths. Let's consider UK, Australia, New Zealand and US whose testing rates are almost same—they are conducting 50,000 to 60,000 tests per million population. As on May 30, fatality rates in Australia and New Zealand were just seven and eight per million, whereas the figures were a massive 944 for the UK and 622 for the US. While the Oceania countries have managed to keep their rates of infection at around 500, it has crossed 10,000 in US and reached 6,707 in UK.

This shows there are other factors that play a critical role in winning the battle than just widespread testing.

BATTLE-READY

From sophisticated techniques to easy-to-use strips, the world has deployed all kinds of tools to fight COVID-19

RT-PCR

MEDICAL PROFESSIONALS vouch for the accuracy of Reverse Transcription Polymerase Chain Reaction when it comes to diagnosis of infectious diseases. The test is based on PCR technique, which replicates genetic material of the pathogen and helps identify it. But PCR is customised to replicating DNA and for pathogens where the genetic material is RNA, as is the case of SARS-CoV-2, an additional step of converting the RNA into DNA is added. This step is Reverse Transcription. After a sample of mucous is collected from the nasopharynx using a swab, it is kept in a buffer solution which also helps in extraction of the virus. Then, using RT-PCR, its genetic material is replicated many times over—usually 40 times. During the replication process, primers (which are specific to the viral genetic material), enzymes, nucleotides and fluorescent probes are added. The fluorescent probes offers a visual signal as soon as a strand is successfully copied. The test is thus also called as real-time RT-PCR (rRT-PCR or qRT-PCR, where q stands for quantitative).

- Looks for viral genes
- Takes 6 hrs
- Conducted in labs with high biosafety levels, BSL-2

Automated RT-PCR

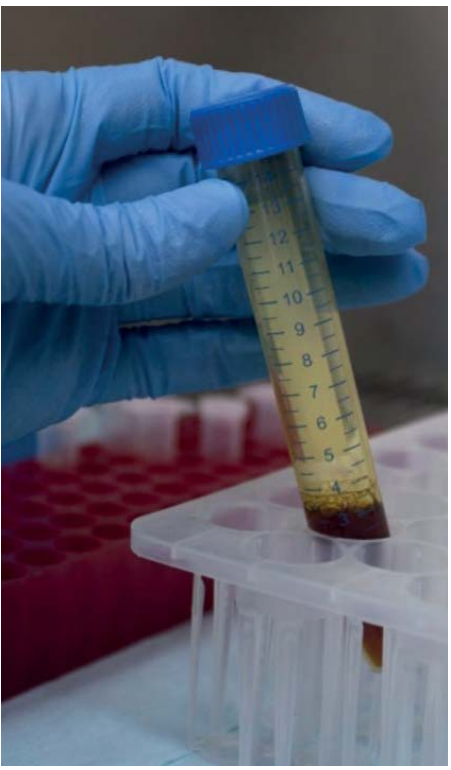
RT-PCR test can also be automated. India has so far allowed two such tests which run on proprietary machines: TrueNat, by Molbio Diagnostics of India, and Xpert® Xpress, by Cepheid of USA. Both were originally used to test for TB. **TrueNat** was approved for COVID-19 by ICMR on April 4. Its battery-operated kits are the size of a telephone and can be taken out into the field to test as many as 15 individuals a day. ICMR allowed the use of **Xpert® Xpress** on April 19 under emergency use authorisation. The test is fully automated and provides the results in 45 minutes. Four tests can be performed simultaneously. Both tests require positive results to be confirmed by RT-PCR.

- Looks for viral genes
- Takes 35-50 minutes
- Conducted in BSL-2 labs, portable
- Positive results have to be confirmed by RT-PCR

Antibody tests

THESE CAN be manual or automated immunoassays. They identify the IgM and IgG antibodies developed against the SARS-CoV-2. For the test, whole blood, serum and plasma can be used and if antibodies are present in the sample, these bind to the antigen immobilised on the test strip and give a coloured reaction. Such test kits are easy to use, provides quick results and are also effective in identifying asymptomatic patients. There is a risk of getting false positives and results need to be confirmed using a more advanced test. In case of **ELISA**, (enzyme-linked immunosorbent assay) antibody test, as many as 90 tests can be run simultaneously. The results are more reliable than strip tests and can also provide quantitative data. The test provides results in around 2.5 hours.

- Looks for antibodies
- Takes 20 minutes to 2.5 hrs
- To be conducted under doctor's supervision
- Useful only for experimental or surveillance purposes



Antigen rapid tests

ANTIGEN IS a foreign substance produced by a pathogen, which induces an immune response in the body, especially the production of antibodies. The technique thus detects the presence of antigen or viral RNA in the sample. The test is being developed by E25Bio, a Massachusetts-based biotech startup. The test relies on a patient's nasopharyngeal swab. It resembles an over-the-counter pregnancy test and provides visual results within 15 minutes by detecting the presence of the virus in the sample. The company is in the process of obtaining clearance under USFDA's emergency use authorisation model. Another company, OraSure Technologies Inc, has also received funds to develop a kit based on this technique.

- **Looks for viral genes**
- **In development stage**

CRISPR

THIS TEST identifies the virus using the CRISPR genome editor, which uses tags that carry enzymes to the target DNA and cut it. For identifying the virus, a special tag has been developed whose enzyme, instead of cutting the gene, gives off a signal that it has reached the target. A diagnostic kit based on CRISPR received emergency use authorisation by USFDA on May 7. Sherlock™ CRISPR SARS-CoV-2 kit is based on the specific high sensitivity enzymatic reporter unlocking technique. The genetic material is extracted from the patients' sample, amplified and incubated and detected with Cas13 enzyme. A commercially available paper dipstick is then used to confirm the presence of the virus with the naked eye. A similar kit, DETECTR™, is being developed by Mammoth Biosciences and UC San Francisco.

- **Looks for viral genes**
- **Takes 30 minutes**
- **As accurate as RT-PCR**

Dogs

This experiment involves training dogs to sniff out people suffering from COVID-19. The three-month trials would be led by the London School of Hygiene & Tropical Medicine and are backed with £500,000 of government funding. The UK hopes these dogs would be part of the country's strategy to test people. Each dog is expected to screen as many as 250 people every hour. The dogs would include breeds like labradors and cocker spaniels. Dogs are already used to detect a host of diseases such as cancers and malaria. The dogs use specific odour that a sick person gives out. Samples of breath and body odour can come from a number of sources like used face masks.

- **Looks for odour**
- **Under trial**
- **Can test 250 people per hour**

TO TEST OR NOT

As India begins to relax lockdown rules, there is a growing demand for tests on a mass scale. But it might not help

WITH DENSELY packed cities, widespread malnutrition and a rickety health infrastructure, India has little margin for error when it comes to handling the COVID-19 pandemic. But so far, the two things that have helped the country from a tsunami of cases are its past experience and staying nimble, says the Indian Council of Medical Research (ICMR). "We learned from the 2009 Swine flu epidemic," it says in a recently released *Intelligent Testing Strategy*. Then only two institutes—the National Institute of Virology and the National Centre for Disease Control—had the capacity to perform molecular tests essential for pathogen diagnosis. But now, there is a network of virus research and diagnostic laboratories (VRDL), 13 of which were roped in for testing in cities with international airports even before the country reported its first cases.

Imposing nationwide lockdown, dubbed the biggest and stringent, is also part of this testing strategy, ICMR says. This provided time to create adequate facilities to trace, track, test, quarantine and treat before the disease spread uncontrollably. As on May 28, at least 641 public and private laboratories and those in research and development institutions, universities and public and private medical colleges have been roped in to ensure that the load of testing does not overwhelm the system at any time. At places where these could not be provided, a system to transport samples to the nearest testing facility has been set up or automated machines like TrueNat have been provided, says the document.

The government has also been revising its testing guidelines to iron out glitches as the pandemic spreads and throws new challenges (see 'Staying nimble...'). Today, India has the capacity to test around 0.14 million samples a day, which the government plans to ramp up to 0.2 million. At least 35 developers, including 20 domestic ones, are providing RT-PCR kits. While antibody tests are not part of the guidelines, they too are being employed in the country and supplied by 15 developers, including 10 domestic ones. Using rapid test kits, on May 12, ICMR initiated a community-based serological survey to estimate the prevalence of COVID-19 in the population. It is also carrying out a hospital-based surveillance to monitor the trend of infection in all districts.

THE PREVALENCE OF CASES DOES NOT INCREASE WITH THE INCREASE IN THE NUMBER OF TESTS, OF COURSE BARRING HOT SPOTS IN CITIES AND IN SOME DISTRICTS THAT REPORT HIGH INFECTION

In the absence of treatment, these tests would not be of any help to patients, but the data helps understand the progress of the pandemic. For instance, online database *ourworldindata.org* that provides information on the number of tests a country conducts to find one COVID-19 case, says most countries see a fall in the ratio as their outbreaks grow. Once the number-of-tests-to-positive-case ratio starts rising again, it suggests that country has controlled the pandemic. As per the database, as on March 13, India was conducting 86.667 tests to find one case, meaning fewer people were infected. This number has gradually been going down and on May 26, it was as low as 21.503, suggesting that India is heading towards the peak of the epidemic.

In India, the level of testing is low. On May 26, it performed 0.075 tests per 1,000 population, which is way lower than the 1.167 tests by the US per 1,000

^ States like Bihar and Odisha have deployed thermal screening and RT-PCR tests to detect infections among returning migrant workers

population. Public health experts, however say widespread testing might not provide much insight into COVID-19 prevalence or help contain it. Russia for instance, performed 11,603.5 tests to find one positive case on March 5 and then 12,841.5 tests for one on the very next day. However, this high level of testing did not help the country, which is now the third worst-hit by the pandemic. On May 26, it reported one new case per every 25.919 tests performed.

K R Antony, Kochi-based public health consultant and former director of the State Health Resource Centre, Chhattisgarh, says, "In India a seven-fold increase in testing after March 27 at the national level did not have a corresponding increase in positive cases. Of the total test samples, positive cases continued to hover around 3.9 per cent. This suggests the prevalence of

PHOTO: REUTERS

STAYING NIMBLE IS KEY

India has been changing its testing guidelines as pandemic spreads and throws new challenges

FIRST GUIDELINE MARCH 17

Fourteen-day home-quarantine for asymptomatic people after international travel; test if they develop symptoms like fever, cough and difficulty in breathing; isolate them and treat as per protocol if test result is positive.

Home-quarantine all contacts of lab-confirmed positive cases; test if they become symptomatic; isolate and treat if they are positive.

Test healthcare workers managing respiratory distress or Severe Acute Respiratory Illness (SARI) if they show symptoms.

ADDITIONS MARCH 20

Test all hospitalised patients with Severe Acute Respiratory Illness.

Test all direct contacts of confirmed cases within 5-14 days of contact

ADDITIONS APRIL 9

Test within 5-14 days all those who came in contact with a confirmed case at hotspots and clusters and in large migration gatherings and evacuees centres.

All those showing influenza-like illnesses like fever, cough, sore throat, runny nose should be tested within 7 days of illness with RT-PCR. After 7 days, they should be provided with an antibody test. Negative result to be confirmed with RT-PCR.

ADDITIONS MAY 18

Test hospitalised patients who develop symptoms with influenza-like illnesses.

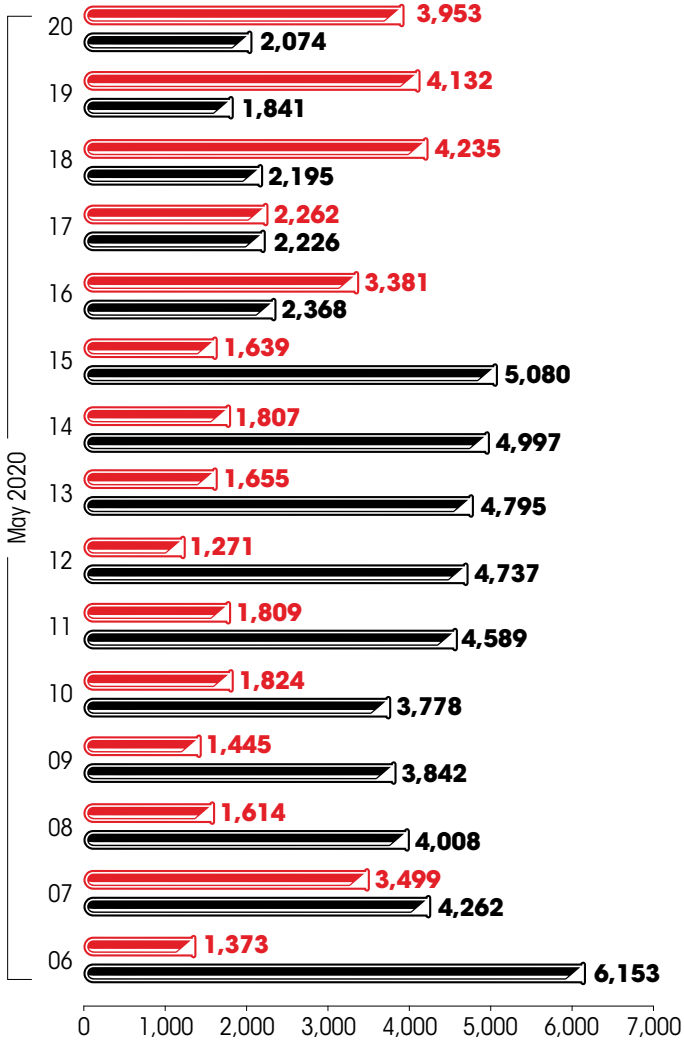
Test returnees and migrants with influenza-like illnesses within 7 days.

No emergency procedure (including deliveries) be delayed for lack of test. However, samples can be sent for testing.

Backlog burden

An analysis of COVID-19 diagnosis in Delhi shows on most days in May pending tests exceeded the samples tested

00 Samples tested **00** Samples pending



Source: Department of Health and Family Welfare, Government of National Capital Territory of Delhi

cases does not increase with the increase in the number of tests, of course barring hot spots in cities and districts that report high infection. In fact, the more we widen the net of sample collection to the general population the lower will be the positivity rate," he says. This is particularly true for India where almost half of the districts are not affected by the pandemic.

"Due to the complexity of the disease in terms of high proportion of asymptomatic cases and the uncertainty surrounding the testing and its validity, sole dependence on testing and seeing it as a magic bullet to the problem of COVID-19 is incorrect," says Mathew George, professor at the Centre for Public Health, Tata Institute of Social Sciences, Mumbai. The age of the patient, co-morbidities, whether symptomatic or asymptomatic, occupation, staying single or with a family of elders—all these factors decide the course of action more than the test results, he adds.

Gaps in the pandemic control system can also lead to spread of the disease. Consider the national capital Delhi, which has 32 labs—15 are government-run and 17 privately owneed. Following a Delhi high court order on May 4, Delhi has been putting all data related to daily tests, positive cases and pending cases in the public domain. A quick analysis of these data shows massive backlogs. There are days when the backlogs match the number of tests done that day (see 'Backlog burden'). Other than infrastructure, shortage of technicians is a reason for such backlogs. "This is because no earlier planning was done for such type of viral pandemic in India," say A R Deshmukh and S N Bhattacharjee, of Delhi-based All India Medical Laboratory Technologist Association.

Besides, the cost of performing the test for a large majority of people who have not been exposed to the coronavirus could be prohibitive in a country, whose per capita expenditure on public health in 2018 was ₹1,657—way less than RT-PCR test which costs ₹4,500. Understandably, the govern-ment is trying to reduce the testing burden. On April 13, in areas with low prevalence of COVID-19, ICMR said pooled samples (genetic material from five patients) could be tested using RT-PCR. In this, all patients need to be tested only if the pooled sample tests positive. However, the desperation of several other countries is not limited to cost-cutting.

ULTIMATE CURE?

The idea that those who have had COVID-19 will, indeed, be immune to the virus is fraught with scientific, ethical and legal issues

^ Doctor extracts mucous sample using a swab at a newly installed Walk-In Sample Kiosk in a government-run hospital in Chennai. India faces an acute shortage of testing kits for diagnosing COVID-19

PHOTO: REUTERS

IMMUNITY OFFERS hope and reassurance. So, governments worldwide are desperate to identify those who have recovered and developed antibodies against SARS-COV-2. Some say this could serve as the basis for an "immunity passport" that would enable individuals to travel or to return to work assuming that they are protected against re-infection. Chile is poised to become the first country to provide such certificates to recovered COVID-19 patients, which will be valid for three months.

In March, Germany tested its population for immunity against COVID-19 using the rapid test kit. In Gangelt municipality, 14 per cent of the 500 people tested were found to have antibodies against SARS-COV-2. Swab tests showed 2 per cent were sick. Based on the findings, Germany planned to conduct serological tests across the country to issue immunity certificates so that people could resume work. But on May 5, it decided not to go ahead unless the study is cleared by its ethics council.

Alexandra L Phelan, professor at the microbiology and immunology department and an adjunct professor of law at the

Georgetown University Law Center, the US, wrote in *The Lancet* on May 4 that the potential discriminatory consequences of immunity passports might not be expressly addressed by existing legal regimes, because immunity from disease (or lack thereof) as a health status is a novel concept for legal protections. In their column in *New York Times*, Kenneth Roth, executeive director of Human Rights Watch, and Annie Sparrow, a critical-care pediatrician and assistant professor of population health science and policy at the Icahn School of Medicine at Mount Sinai, usa, wrote that employers might insist on antibody certificates simply to minimise absenteeism or medical costs among their workers; employees might find it easier to work with colleagues who have antibody certificates rather than to continue with face masks and social distancing.

But in this fight some are willing to make sacrifices. These are the countries that hope to achieve "herd immunity" naturally. The debate around their quest is so intense that "herd immunity" along with 30-odd other words and phrases related to the pandemic has made its way into *Oxford Dictionaries* (online version) in recent weeks. The dictionary defines herd immunity as "protection from a disease that happens if a large percentage of the population is immune to it." Proponents believe once adequate immunity develops in a population, the spread of COVID-19 would stop. Vaccines are usually used to create such herd immunity against infectious diseases like measles, mumps, polio and chickenpox.

But can we actually bank on our own immunity system to tide over the pandemic? If yes, to what extent?

Researchers are racing against time to find the answers. An analysis by the Center for Infectious Disease Research and Policy, US, made public on April 30, says COVID-19 is not likely to be halted until 60 to 70 per cent of the population is immune. However, studies on isolated populations shows no city has so far managed to achieve this magical state.

WHO'S IMMUNE

60-70%

of population must develop immunity against COVID-19 to halt the pandemic.

SO FAR

no city has achieved this magical state.

New York city, US
19.9%

London, UK
14.8%

Madrid, Spain
11.3%

Boston, US
9.9%

Stockholm, Sweden
7.3%

Barcelona, Spain
7.1%

Santa Clara, US
4%

Los Angeles, US
2.8-5.6%

Note: Figures for Santa Clara, Los Angeles for April; rest for May; Sources: Government reports; *study by Stanford University, US, researchers published on MedRxia on April 30; **press release by University of Southern California, April 20

In Spain, the fourth worst-hit nation in the pandemic, the government launched a rapid serology test on April 27 to gauge the exposure of people to SARS-COV-2. It found only 11.3 per cent and 7.1 per cent people have developed antibodies against COVID-19 in Madrid and Barcelona, which have paid the highest price in fatalities.

In the last week of April, New York city, the epicentre of the pandemic in the US, also launched an antiobody study by testing 15,000 people at grocery stores and community centers across the state. Its findings show 12.3 per cent people now have COVID-19 antibodies. A similar study by the city government of Boston, in Massachusetts state of the US, finds 9.9 per cent people have antibodies against COVID-19. In UK, the COVID-19 Surveillance Report shows that 14.8 per cent people in London had antibodies against COVID-19.

Sweden, which has not imposed lockdown, is hopeful that herd immunity would see it through the pandemic. When COVID-19 broke out there towards the end of February, the government issued guidelines banning gatherings of over 50 people. Restaurants, schools and parks remained open. It estimated that in Stockholm 60 per cent people would develop antibodies against the virus by May-June. But its Public Health Agency says only 7.3 per cent people have developed antibodies by the end of April. Speaking to local media, Anders Tegnell, the country's chief epidemiologist and brain behind the strategy, has said, "Either the calculations made by the agency and myself are quite wrong...or more people have been infected than developed antibodies."

Naturally developed immunity following a sickness is dicey. Even if adults develop immunity against the disease—a study posted on *medRxiv* on March 30 says older patients develop more antibodies against COVID-19 than the younger ones—it can circulate among children and infect those with weakened immune systems. Besides, there is no evidence to show how

long the immunity would protect from COVID-19. Other viruses like the flu mutate over time. So antibodies from a previous infection provide protection for less than a year. In case of COVID-19, many patients who tested negative after treatment are testing positive again. As per one theory, these people getting reinfected might have developed low immunity during the first round of infection. But there is no conclusive evidence on this. When researchers from China tried to reinfect the rhesus monkeys recovered from COVID-19 infection, they did not succeed. The monkeys developed immunity against the disease, says a study published on preprint server *bioRxiv* on March 13. However, researchers at Fudan University, Shanghai, who studied blood samples from COVID-19 patients released after treatment, found nearly a third had low levels of antibodies. In some patients, antibodies could not be detected.

A review by the Norwegian Institute of Public Health has also found limited evidence on immunity after infection with SARS-cov-2. "Two studies showed sustainable immunoglobulin G (IgG is an antibody) levels one to two years after SARS-cov infection, but it is uncertain whether this finding can be generalised to SARS-COV-2," notes the document published in April.

A paper published in *Immunity* on May 3, however, sheds some light on how antibodies behave in people who had recovered from COVID-19. It compared the immune responses of 14 patients—eight recently discharged with six follow-up patients. When compared with healthy controls, all recovered patients had higher levels of antibodies against COVID-19. But when compared among themselves, newly discharged patients had more antibodies than follow-up patients. But for how long would this immunity last? Will they get reinfected if exposed to high quantities of virus or their physical state weaken? Scientists do not have answers to these probing questions so far.

It seems we have to live with the virus for some time even after a vaccine is ready.

BESIDES, THERE IS NO EVIDENCE TO SHOW HOW LONG THE IMMUNITY WOULD PROTECT FROM COVID-19. OTHER VIRUSES LIKE THE FLU MUTATE OVER TIME. SO ANTIBODIES FROM A PREVIOUS INFECTION PROVIDE PROTECTION FOR LESS THAN A YEAR

Vaccines do not provide 100 per cent immunity. Flu vaccine, for one, is 59 per cent effective in adults and 27 per cent in keeping a person out of a hospital. A 2012 review says BCG vaccine, primarily used against tuberculosis, was 60 per cent effective in the first five years after inoculation. The effectiveness decreased to 56 per cent between five and 10 years and to 46 per cent for up to 15 years. But vaccines against diphtheria are effective.

The COVID-19 vaccine has been put on a fast track and there are chances that it might not be tested very robustly. This can pose a serious risk. In an interview with US-based natural health activist Joseph Mercola, Robert Kennedy Jr, an environmental lawyer and anti-vaxxer, narrates the problems with vaccines against coronavirus. He says they trigger the production of two kinds of antibodies. While neutralising antibodies help fight the disease, the binding ones make the body more vulnerable. In 2012, four vaccines were tested on ferrets who showed good antibody response. But when they were exposed to the wild virus, they died. This again happened in 2014 when dengue vaccine DENVax was administered on children in the Philippines. When they got infected with dengue, 600 of them died.

However, some communities may have an advantage over others when it comes to immunity. This natural defence mechanism of the body trains itself and evolves as people get constantly exposed to pathogens. Being challenged daily with diseases like tuberculosis, malaria, dengue and chikungunya, Indians are more immune to infections compared to several other nationals. There is also evidence that Indians have evolved to gain more genes that protect them against viral infections.

"These genes enable natural killer (NK) cells, a type of white blood cells in our body that provide a first line of defense against viral infections," says Rajalingam Raja, director of Immunogenetics and Transplantation Laboratory at the University of California in San Francisco,

US. Two families of genes, KIR genes and HLA genes, play a part in this protective function. Indians have more KIR genes than the Chinese and caucasians, says Raja in an article in *Genes and Immunity* in 2008. He says Indians have also evolved to gain unique genes that regulate T and B cells, which produce specific and long-standing immunity to infection and could make Indians more immune to SARS-COV-2. However, the authorities cannot take a decision on easing the lockdown based this special immunity of citizens. As Raja says, the number and type of genes are highly variable between individuals. "We do not know which gene is protecting from the SARS-COV-2 infection."

So, how to live with it?

COVID-19 remains a big unknown. The only evidence we have is it is highly infectious and has a fatality rate 10 times higher than that of flu

But we still do not know of all its symptoms and have little understanding about its long-term health impacts. So most researchers are in favour of taking precautions. "We should maintain the current levels of infection or even reduce the levels until a vaccine becomes available. This will take some level of continued physical distancing for an extended period, likely a year or longer, before a highly effective vaccine can be developed, tested and mass produced," says Gypsyamber D'Souza, epidemiologist with the Johns Hopkins Bloomberg School of Public Health, US. But waiting for this vaccine might not make much sense for countries like India, which have pathetic vaccine coverage—as per the National Family Health Survey of 2015-2016, the percentage of fully immunised children ranged from 91.3 per cent in Puducherry to 35.7 per cent in Nagaland.

As of now, the virus seems unstoppable, stirring second wave in countries like South Korea that had contained it the first time. The way to go ahead would be to have a mix of testing, physical distancing, imposing quarantines and lockdowns, and ensuring sanitation and healthcare, but all implemented at the correct time and as per the need. Analyst Joe Hasell at *ourworldindata.org* compares testing strategies followed by South Korea, Italy, UK and US. All these reported their first cases in January. While South Korea tested early, monitored the outbreak and managed to curb it, Italy, UK and US focussed on testing quite late, resulting in runaway cases. New Zealand too followed the "go hard, go early" approach despite inadequate infrastructure to contain the pandemic. Its prime minister Jecinda Ardern now claims that the country is on track to eliminate the virus. Australia, which ranks among countries that have succesfully fought against COVID-19 despite moderate restriction measures, allowed local governments to impose lockdowns while ramping up health infrastructure.

BEING CHALLENGED DAILY WITH DISEASES LIKE TB, MALARIA AND DENGUE, INDIANS ARE MORE IMMUNE TO INFECTIONS COMPARED TO SEVERAL OTHER NATIONALS. THERE IS ALSO EVIDENCE THAT INDIANS HAVE EVOLVED TO GAIN MORE GENES THAT PROTECT THEM AGAINST VIRAL INFECTIONS

To help people return to normality while keeping the virus under control, the focus is now more on localised and targeted measures. On May 28, the UK has launched the Test and Trace service, with 25,000 contact tracing staff and the capacity to trace the 100,000 contacts per day. Its idea is to ensure that the R0 number remains lower than 1 such that one infected person does not infect more than one person. While the infected person would be tested, an intensified effort would be on to trace down their contacts who would then be asked to self-isolate for 14 days. This would reduce the need to quarantine and lockdown large areas. Scotland and Northern Ireland too have have introduced similar systems of test, trace and break the chain strategy.

To deal with the pandemic, the world needs to urgently innovate and change the way it deals with diseases. While the health infrastructure needs to be made robust, not only in one country but across the world, health care requires more than just tests and ventilators. It requires identifying what strategy works where and when as the battle is not going to be over anytime soon.

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