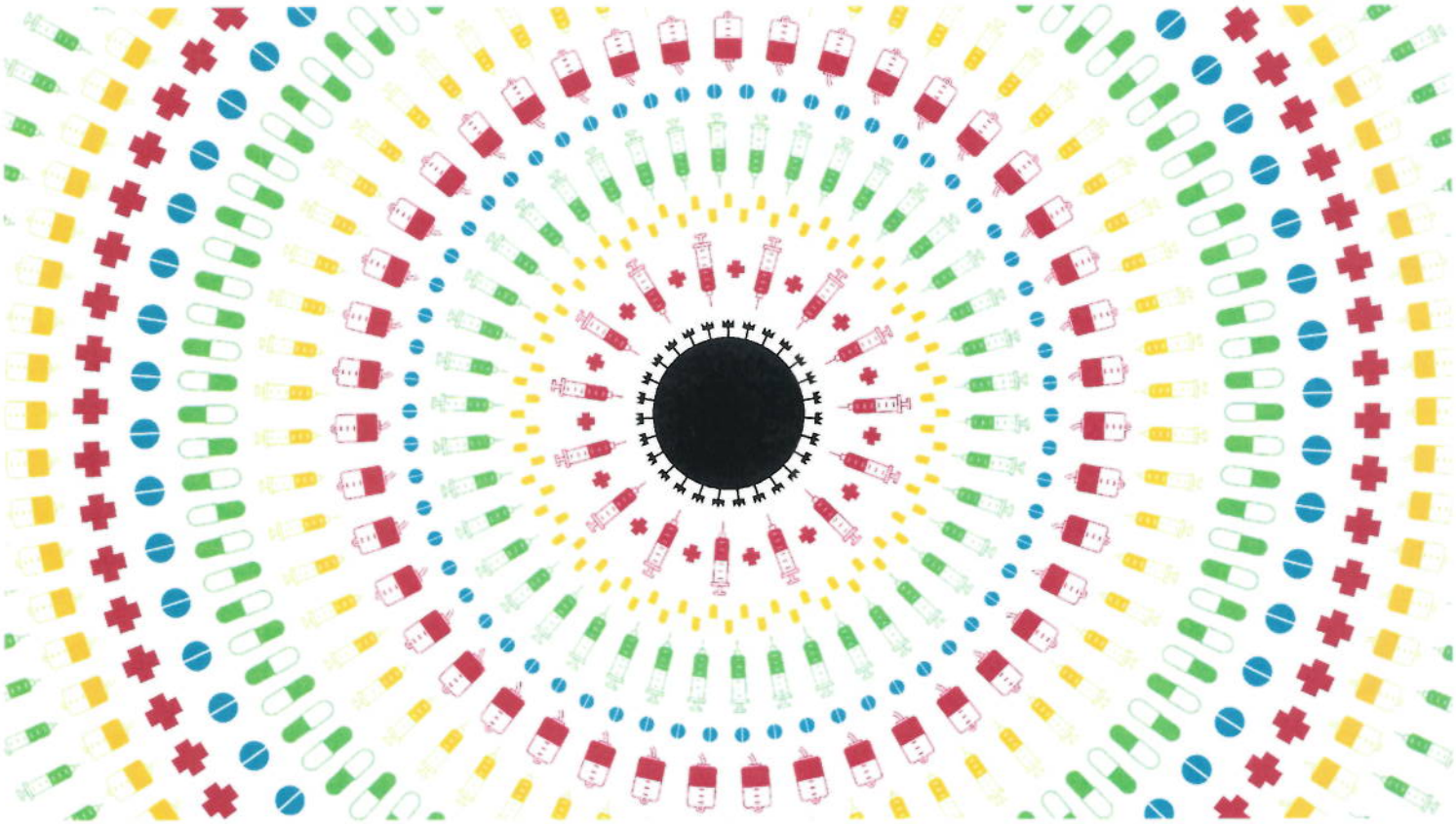


The lifeline pipeline

By **Christine Soares**
Published: **April 13, 2020**
Updated: **May 12, 2020**

With much of the world living in lockdown, the spread of the new coronavirus, SARS-CoV-2, that was first detected in China late last year is beginning to slow in some places. As of May 13, 4.3 million had been infected and 290,000 killed by COVID-19, the disease caused by the virus.

While a safe, effective vaccine is still more than a year away, researchers are rushing to repurpose existing drugs and non-drug therapies as well as testing promising experimental drugs that were already in clinical trials.

Even moderately effective therapies or combinations could dramatically reduce the crushing demand on hospitals and intensive care units, changing the nature of the risk the new pathogen represents to populations and healthcare systems. New drugs, together with new diagnostics, antibody tests, patient- and contact-tracing technologies, disease surveillance and other early-warning tools, mean the anticipated next 'wave' of the global pandemic does not have to be nearly as bad as the first.

Spotlight: Latest in COVID research - May 11

Click for more information

Men's blood contains more of enzyme that helps coronavirus infect cells

Adding interferon may boost effectiveness of coronavirus treatment

UK coronavirus study reassures pregnant women; Swedish study says don't downplay risks

More than 70 vaccine candidates are also in development around the world, with at least five in preliminary testing in people. Here are some of the drugs, vaccines and other therapies in development:

GILEAD

Remdesivir

TYPE
DRUG

STATUS
REPURPOSED
EXPERIMENTAL

EARLY RESULTS
0-3 MONTHS

Antiviral drug given by infusion previously failed as an Ebola treatment but showed promise against certain coronaviruses in animal studies. In the first large, randomized COVID-19 trial, remdesivir led to a statistically significant reduction in recovery time of hospitalized patients compared with a placebo, demonstrating that it does impact the virus. Based on that data, the FDA issued an emergency use authorization for the drug despite mixed results from other smaller studies. More than a dozen trials underway in China, Europe and the United States with further data expected later this month.

CAVEATS

Initial data is expected to come from studies of patients with relatively severe COVID-19.

FURTHER READING

Explainer: What does new data say about Gilead's experimental coronavirus drug?

Data on Gilead drug raises hopes in pandemic fight, Fauci calls it 'highly significant'

Regeneron, Sanofi arthritis drug may only help critical coronavirus patients: study

Report says COVID-19 patients respond to Gilead's remdesivir, shares surge

Two thirds of COVID-19 patients improve after Gilead drug: NEJM

Clinical Trials
New England Journal of Medicine, April 2020

ABBVIE

Kaletra (lopinavir/ritonavir)

TYPE
DRUG

STATUS
REPURPOSED

EARLY RESULTS
0-3 MONTHS

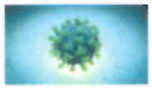
Antiviral combination used to treat and prevent HIV infections. More than 20 trials around the world are testing the therapy as a COVID-19 treatment or for post-exposure prevention for those with high-risk close contact with infected people. Initial results expected as soon as May 2020.

CAVEATS

One randomized controlled trial in China found no differences in viral load or 28-day mortality among 199 patients, according to results published in March. Median time to clinical improvement was one day shorter in patients taking the drug. However, the same doctors at Jinyintan Hospital in Wuhan said in April that they believe Kaletra, as well as a second drug, bismuth potassium citrate, helped some of the COVID-19 patients they treated.

FURTHER READING

WHO sees 'potentially positive data' in treating coronavirus



Key China coronavirus hospital says HIV drug beneficial to patients

Mylan waives exclusive U.S. distribution rights for potential COVID-19 therapy

Clinical Trials
New England Journal of Medicine, March 2020

Hydroxychloroquine / chloroquine

TYPE
DRUG

STATUS
REPURPOSED

EARLY RESULTS
0-3 MONTHS

An old malaria drug that also treats lupus and rheumatoid arthritis is believed to have antiviral as well as anti-inflammatory activity. Blocked the novel coronavirus' (SARS-CoV-2) entry into cells in an in-vitro experiment. In one small French study, some COVID-19 patients showed improvement but there was no way to know if the drug was the reason. Results published in April from another study in France and one in China found no benefit in patients treated with the drug. Dozens more clinical studies are underway around the world.

CAVEATS

Health experts caution it should never be used without a prescription and could lead to dangerous side effects on the heart.

FURTHER READING

Malaria drug touted by Trump for coronavirus fails another test

U.S. FDA warns against malaria drugs Trump championed for COVID-19

Novartis to test efficacy of old malaria drug against COVID-19

Special Report: Doctors embrace drug touted by Trump for COVID-19, without hard evidence it works

Clinical Trials
Journal of Zhejiang Univ (Med Sci), March 2020
Médecine et Maladies Infectieuses, March 2020
Nature, February 2020

UNIVERSITY OF AARHUS, DENMARK; UNIVERSITY OF TOKYO; YALE UNIVERSITY

Camostat mesylate

TYPE
DRUG

STATUS
REPURPOSED

EARLY RESULTS
0-3 MONTHS

Protease inhibitor licensed in Japan and South Korea to treat chronic pancreatitis. In vitro experiments found it blocks a mechanism SARS-CoV-2 uses to enter human cells. A phase 2a trial launched in early April by Aarhus University will examine 30-day changes in disease severity and mortality, with results expected by December 2020. The University of Tokyo also plans a trial of camostat mesylate and a related drug, nafamostat mesylate. A Yale trial in outpatients who test positive for SARS-CoV-2 will look at whether the drug keeps viral loads low, which could help prevent mild illness from becoming severe. That could also make it a good prophylactic. A long safety track record adds to this drug's appeal.

FURTHER READING

Clinical Trials
Cell, March 2020
University of Tokyo, March 2020

ROCHE

Actemra (tocilizumab)

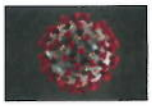
TYPE
DRUG

STATUS
REPURPOSED

EARLY RESULTS
0-3 MONTHS

Monoclonal antibody approved for rheumatoid arthritis and also used to treat a dangerous overreaction of the immune system called a "cytokine storm" in cancer patients receiving a type of therapy that can trigger that response. COVID-19 triggers a similar response in some patients who have fared poorly. Actemra targets interleukin-6 (IL-6), which is believed to play a role in inflammation. Registered trials in China, Europe and the United States are testing it on COVID-19 patients alone or in comparison to other therapies. One French trial is looking at 28-day effects on COVID-19 in patients with advanced cancer.

FURTHER READING



Coronavirus drug hopefuls are cheap to make but may be in short supply

Cancer/COVID-19 Clinical Trial
Clinical Trials

SANOFI, REGENERON PHARMACEUTICALS

Kevzara (sarilumab)

TYPE
DRUG

STATUS
REPURPOSED

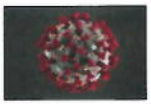
EARLY RESULTS
0-3 MONTHS

Monoclonal antibody approved for rheumatoid arthritis that targets (IL-6). In trials against the cytokine storm immune response in severely ill COVID-19 patients. Early results announced in late April suggest a benefit in the most critically ill patients.

CAVEATS

Based on review of early data showing little benefit for patients who were severely ill but not in critical condition, the companies announced they would continue the trial only in critical patients.

FURTHER READING



Regeneron, Sanofi arthritis drug may only help critical coronavirus patients: study

Exclusive: Sanofi can produce millions of doses of potential coronavirus drug - CEO

Sanofi, Regeneron expand testing of potential coronavirus treatment

Clinical Trials

NOVARTIS, INCYTE

Jakavi (ruxolitinib)

TYPE
DRUG

STATUS
REPURPOSED

EARLY RESULTS
0-3 MONTHS

From a class of drugs known as JAK inhibitors, Jakavi is approved to treat the rare bone marrow cancers myelofibrosis and polycythemia vera and is in late-stage development as a cream for atopic dermatitis. Trials in Canada and Mexico will test the drug in COVID-19 patients with severe pneumonia associated with the cytokine storm immune response, with preliminary results expected by June 2020. In the United States, Novartis established a managed access program for use in severe/very severe COVID-19 illness on April 7.

FURTHER READING

Novartis, Incyte join repurposing wave to give Jakavi a trial run in COVID-19

Clinical Trials

MODERNA/NIAID

mRNA 1273

TYPE
VACCINE

STATUS
EXPERIMENTAL

RNA vaccine made with messenger-RNA (mRNA) encoding the spike protein on the surface of the new coronavirus (SARS-CoV-2) and delivered via a lipid nanoparticle. The phase 1 trial with 45 subjects aged 18 to 55 at three locations in the United States will evaluate the vaccine's safety and provide early data on the immune response it induces. Trial completion is anticipated to be June 1, 2020.

EARLY RESULTS
0-3 MONTHS

FURTHER READING

Moderna's potential coronavirus vaccine gains FDA's 'fast track' status

Special Report: Countries, companies risk billions in race for coronavirus vaccine

J&J, Moderna sign deals with U.S. to produce huge quantity of possible coronavirus vaccines

Clinical Trial

Convalescent plasma

TYPE
NON-DRUG THERAPY

EARLY RESULTS
0-3 MONTHS

Blood plasma from recovered COVID-19 patients is transfused into patients who are currently ill, in the hope that freshly-made antibodies will help fight the virus. The method has been used for more than 100 years and carries little risk of harm or side effects. Small case studies suggest it may help reduce virus levels, and controlled trials are in progress in China, Europe and the United States to gather stronger evidence of a benefit. Results published in April from a study in 10 patients with severe illness in China found significant improvement compared to similar patients who did not receive the treatment.

CAVEATS

Already in limited use, the supply of plasma from recovered patients may not be sufficient to meet all needs. Further studies of recovered patients will determine if everyone produces a full immune response to the infection, including "neutralizing antibodies," at sufficiently high levels to become donors.

FURTHER READING

Why U.S. hospitals see promise in plasma from new coronavirus patients

Grifols says anti-coronavirus hyperimmune immunoglobins may be ready mid-July

UK to trial use of COVID-19 survivors' blood plasma for treatment

Clinical Trials

CHONGQING PUBLIC HEALTH MEDICAL CENTER, CHONGQING SIDEMU BIOTECHNOLOGY TECHNOLOGY CO.,LTD.

NKG2D-ACE2 CAR-NK cells

TYPE
NON-DRUG THERAPY

STATUS
EXPERIMENTAL

EARLY RESULTS
0-3 MONTHS

NKG2D receptor for the immune system's natural killer (NK) cells that play a major role attacking foreign invaders like cancer or viruses, paired with the ACE-2 receptor that the coronavirus uses to enter human cells. A multicenter Phase 1/2 trial in 90 patients is testing whether this cell therapy can prevent the SARS-CoV-2 virus from entering cells and multiplying, and will look at efficacy over 28 days in patients with severe or critical COVID-19 pneumonia.

FURTHER READING

Clinical Trial

NOVAVAX

NVX-CoV2373

TYPE
VACCINE

STATUS
EXPERIMENTAL

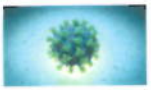
EARLY RESULTS
0-3 MONTHS

Novavax said its Matrix-M adjuvant would be used with the vaccine candidate - NVX-CoV2373 - to enhance immune responses. Trial in 130 adults is expected to begin in mid-May with with preliminary immunogenicity and safety results in July, according to the company.

CAVEATS

Strong immunogenicity in animal tests, but might require two doses in humans, which would limit supply.

FURTHER READING



Novavax to start human trial for novel coronavirus vaccine

With Wuhan virus genetic code in hand, scientists begin work on a vaccine

BIONTECH/PFIZER

BNT162

TYPE
VACCINE

STATUS
EXPERIMENTAL

EARLY RESULTS
0-3 MONTHS

Based on messenger RNA encoding viral proteins, this candidate started trials in Germany in late April, and U.S. trials in early May. Pfizer already collaborates with BioNTech to develop mRNA-based vaccines for influenza. Pfizer has said it hopes to receive emergency authorization from the U.S. Food and Drug Administration for the new vaccine as early as October, and could distribute up to 20 million doses by the end of 2020, with an eye toward producing hundreds of millions of doses next year.

FURTHER READING

Pfizer, BioNTech set to begin U.S. coronavirus vaccine trial

Pfizer aims for 10-20 million doses of coronavirus vaccine by end-2020

Pfizer, BioNTech to co-develop potential coronavirus vaccine

APEIRON BIOLOGICS

RhACE2 APN01

TYPE
DRUG

STATUS
EXPERIMENTAL

EARLY RESULTS
3-6 MONTHS

A recombinant human angiotensin converting enzyme 2 (rhACE2) under Phase-2 clinical development in ALI (Acute Lung Injury) and PAH (Pulmonal arterial hypertension). This synthetic version of the human protein that the novel coronavirus uses to enter cells is being tested in Austria to see if it can block viral entry and decrease viral replication in COVID-19 patients, reducing deaths or the need for mechanical ventilation. Preliminary results from the trial are expected in September 2020.

FURTHER READING

Clinical Trial

SHENZHEN GENO-IMMUNE MEDICAL INSTITUTE

Lentiviral Minigene Vaccines (LV-SMENP)

TYPE
VACCINE

Engineered minigenes encoding viral antigens; lentiviral vector designed to infect dendritic and T cells - key components of the immune system - to induce immunity. The trial in 100 adults in Shenzen, China, is expected to be

STATUS
EXPERIMENTAL

EARLY RESULTS
3-6 MONTHS

complete by July 31, 2020.

FURTHER READING

Clinical Trial

MURDOCH CHILDREN'S RESEARCH INSTITUTE; UMC UTRECHT

BCG tuberculosis vaccine

TYPE
VACCINE

STATUS
REPURPOSED

EARLY RESULTS
3-6 MONTHS

Bacillus Calmette-Guérin tuberculosis vaccine that induces a broad innate immune-system response, which has been shown to protect against infection or severe illness with other respiratory pathogens. Large trials in Australia and the Netherlands are testing whether using BCG to rev-up immune defenses in health workers and the elderly reduces unplanned absenteeism, respiratory illnesses including COVID-19, severe illnesses and deaths. Two additional trials by the Max Planck Institute in Germany of a TB vaccine candidate, VPM1002, are in the works.

FURTHER READING

Explainer: How an old tuberculosis vaccine might help fight the new coronavirus

Clinical Trials

INOVIO PHARMACEUTICALS, COALITION FOR EPIDEMIC PREPAREDNESS INNOVATIONS (CEPI)

INO-4800

TYPE
VACCINE

STATUS
EXPERIMENTAL

EARLY RESULTS
3-6 MONTHS

DNA plasmid vaccine delivered through the skin via a patch-style device using a brief low-voltage electronic pulse to induce cell membranes to open, making them more receptive, in theory, to accepting the vaccine's genetic material. A clinical trial launched on April 3 could yield preliminary data by late summer, according to the company, which has said it can manufacture 1 million doses by year-end for additional trials and emergency use.

FURTHER READING

Clinical Trial

PHARMAMAR

Aplidin (plitidepsin)

TYPE
DRUG

STATUS
REPURPOSED

EARLY RESULTS
3-6 MONTHS

A map of the virus' interactions inside the human body flagged plitidepsin among several compounds that block a key human protein it needs to infect cells. Aplidin, a cancer therapy approved in Australia, had already shown activity against a different coronavirus in lab studies and was about to enter COVID-19 trials in Spain when the protein-mapping study supporting its potential was published in late April.

FURTHER READING

Nearly a dozen approved drugs could be effective against COVID-19: study

Nature, April 2020
PharmaMar, April 2020

INFLARX

IFX-1

TYPE
DRUG

STATUS
EXPERIMENTAL

EARLY RESULTS
6-12 MONTHS

Monoclonal antibody designed to block a mechanism of inflammation. In early April, a trial in the Netherlands launched to test IFX-1 in patients with severe COVID-19 pneumonia, with preliminary results expected in late October 2020. It is also being tested in other inflammatory conditions.

FURTHER READING

Clinical Trial
InflaRx

CANSINO BIOLOGICAL INC./BEIJING INSTITUTE OF BIOTECHNOLOGY

AD5-nCov

TYPE
VACCINE

STATUS
EXPERIMENTAL

EARLY RESULTS
6-12 MONTHS

Non-replicating viral vector. A single-center phase 1 trial with 108 subjects aged 18 to 60 in Wuhan, China, started in March to test the safety and immune responses generated by a recombinant vaccine that uses another respiratory virus, adenovirus, to deliver the vaccine material. On April 12, a randomized controlled phase 2 trial with 500 participants launched to test varying doses against placebo. Phase 1 completion is expected in late December 2020, and phase 2 results are expected in January 2021.

FURTHER READING

Chinese coronavirus vaccine could be tested, manufactured in Canada

Clinical Trial

SANOFI, GSK

Adjuvanted vaccine candidate

TYPE
VACCINE

STATUS
EXPERIMENTAL

EARLY RESULTS
6-12 MONTHS

In mid-April, two of the world's largest vaccine makers announced they would join forces to create and test six candidates built on technologies already proven in flu vaccines. In all candidates, Sanofi's recombinant S-protein COVID-19 antigen will get a boost from GSK's AS03 adjuvant. Scientists and public health experts are already warning that it could be tricky to induce a strong, effective immune response to the SARS-CoV-2 virus, particularly in the elderly and others with weakened immune systems, so the adjuvant enhancement could help. The resulting vaccine might also require just one dose instead of two, which could stretch supplies. The companies plan to start trials in the second half of 2020 and complete development by second half of 2021.

CAVEATS

The ASO3 adjuvant was in GSK's 2009 Pandemrix flu vaccine used in Europe. But only a handful of adjuvanted vaccines are licensed in the U.S., and none containing ASO3. The exception is a flu vaccine approved in 2013 and stockpiled by the U.S. for use in the event of an H5N1 avian flu pandemic.

FURTHER READING

EXCLUSIVE-Sanofi to enroll thousands for its coronavirus vaccine trials

Sanofi CEO warns Europe on cornavirus vaccine race

GSK, Sanofi strike deal to develop COVID-19 vaccine

NEJM, April 2020

IMPERIAL COLLEGE LONDON

Aspirin, Clopidogrel (Plavix), Rivaroxaban (Xarelto), Atorvastatin (Lipitor), Omeprazole (Prilosec)

TYPE
DRUG

EARLY RESULTS
9-12 MONTHS

Trial of cardioprotective drugs to prevent direct damage to the heart muscle that appears to drive the severity of COVID-19 in certain patients, as well as their likelihood of needing invasive critical care. The trial will include more than 3,000 patients in the United Kingdom, with a completion date of March 30, 2021.

FURTHER READING

Clinical Trial

UNIVERSITY OF OXFORD

ChAdOx1

TYPE
VACCINE

STATUS
EXPERIMENTAL

EARLY RESULTS
12-18 MONTHS

Non-replicating chimpanzee adenovirus vector. Phase 1/2 trial with 510 subjects aged 18 to 55 at four centers in the United Kingdom. The trial will test safety and immunogenicity of one or two doses of the vaccine, and is expected to be completed in May 2021.

FURTHER READING

AstraZeneca teams up with Oxford University to develop COVID-19 vaccine

UK scientists to make a million potential COVID-19 vaccines before proof

Epidemic response group ups coronavirus vaccine funding to $23.7 million

Clinical Trial

Diagnostic Testing

TYPE
TESTING

EARLY RESULTS
0-6 MONTHS

Health policy experts say the United States must dramatically increase the availability of tests for the coronavirus if it is to safely reopen its economy. From the start, laboratory-based diagnostic testing has been hampered by shortages of needed materials such as swabs to collect samples and chemical reagents. U.S. regulators have moved speedily to authorize many new commercial tests, but concerns still remain about their accuracy, and some policymakers say entirely new testing technologies need to be developed to fully contain the virus. At present, two types of diagnostic test are available: one looks for the virus' genetic material, or RNA, and the other looks for viral proteins known as antigens. In general, antigen tests have lower accuracy rates than RNA testing.

CAVEATS

Without additional analysis, neither RNA nor antigen tests can tell the difference between active virus, which could infect others, and "dead" viral particles that are no longer contagious. Researchers believe this may explain some cases of recovered patients testing positive for extended periods.

FURTHER READING

Factbox: U.S. COVID-19 tests - What's out there and how well do they work?

U.S. needs better technology to test for COVID-19: top health official

Special Report: How federal snafus slowed testing at a top U.S. hospital

Annals of Internal Medicine, April 2020

ROCHE

Cobas SARS-CoV-2

TYPE
TESTING

EARLY RESULTS
UNKNOWN

Authorized for use by U.S. regulators in March, Roche says it is currently shipping around 8 million tests per month. It requires a sample taken by nasal swab be sent back to a lab for analysis to detect viral RNA. Roche says studies show it can detect very low levels of the virus with 95% accuracy.

FURTHER READING

Switzerland's Roche joins global race to make coronavirus antibody tests

ABBOTT

ID Now

TYPE
TESTING

EARLY RESULTS
UNKNOWN

Approved in late March, Abbott's rapid, point-of-care molecular diagnostic test can provide results on site to patients within minutes. As of May 4, Abbott said it is producing 50,000 of these tests per day, and plans to ramp up to 2 million by June.

CAVEATS

A study conducted by the Cleveland Clinic reportedly showed the test detected the virus in just 85 of 100 samples from patients known to be positive for the virus.

FURTHER READING

Abbott wins U.S. approval for test that can detect coronavirus in minutes

QUIDEL CORPORATION

Sofia 2 SARS Antigen FIA

TYPE
TESTING

EARLY RESULTS
UNKNOWN

Authorized for use in early May, Quidel said this antigen test picks up around 80% of COVID-19 cases.

FURTHER READING

FDA grants emergency use authorization to Quidel for first antigen test for COVID-19

FUJIREBIO

Fujirebio Antigen Test

TYPE
TESTING

EARLY RESULTS
UNKNOWN

It takes about 30 minutes to get a result with Fujirebio's palm-sized antigen test kit, compared with four to six hours for a standard laboratory process known as PCR, according to Japan's health Ministry. Fujirebio can produce 200,000 kits per week, roughly on par with the number of RNA-based diagnostic tests conducted in April in Japan.

FURTHER READING

Japan to approve first coronavirus antigen test kits on Wednesday

Serology / Antibody Testing

TYPE
TESTING

STATUS
EXPERIMENTAL

EARLY RESULTS
0-12 MONTHS

Governments and academic groups have started serosurveys: testing blood for antibodies indicating that a person had been infected by the virus whether or not they had symptoms.

But separate, ongoing research is needed to know what type of antibody neutralizes the virus and what concentration of these in the bloodstream protects against a new infection, as well as whether all infections produce a full antibody response, and how long any protection might last.

Antibody tests take small samples of patients' blood and can be conducted in labs or with on-site tests that provide results in minutes. The FDA recently tightened rules on serological test developers after a proliferation of unauthorized tests raised questions about their reliability. Independent academic groups are also testing the individual tests to assess their accuracy.

CAVEATS

Early data on COVID-19 patients suggests that most develop varying amounts of antibodies in response to infection. One pre-publication report analyzed plasma from 175 patients in China and found that a sign of inflammation correlated with higher levels of antibodies and that younger patients were less likely to produce large amounts of antibodies.

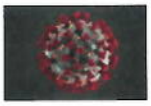
Data is still lacking on whether mild or symptomless infections generate meaningful antibody responses or protection.

FURTHER READING

U.S. targets fraud in coronavirus antibody test market with tighter rules

Broad coronavirus testing crucial in lifting restrictions: U.S. experts

Impossible dilemma? World watches Italy as businesses plead to return to work



Explainer: What are coronavirus antibody tests?

COVID-19 Testing Project
Annals of Internal Medicine, April 2020
Preprint, May 2020
The Lancet Infectious Diseases, March 2020
Preprint, March 2020
Preprint, April 2020

ABBOTT

Architect SARS-CoV-2 IgG Assay

TYPE
TESTING

EARLY RESULTS
UNKNOWN

Researchers at the University of Washington School of Medicine say the test, which Abbott launched in April, has a specificity of 99.9% and a sensitivity of 100%, suggesting very few false positives and no false negatives. Abbott has already shipped more than 10 million antibody tests to hospitals and labs.

FURTHER READING

Study suggests Abbott COVID-19 antibody test highly likely to give correct results

FDA authorizes use of Abbott's COVID-19 antibody test on second system

J. Clinical Microbiology, May 2020

Design and illustration by Maryanne Murray