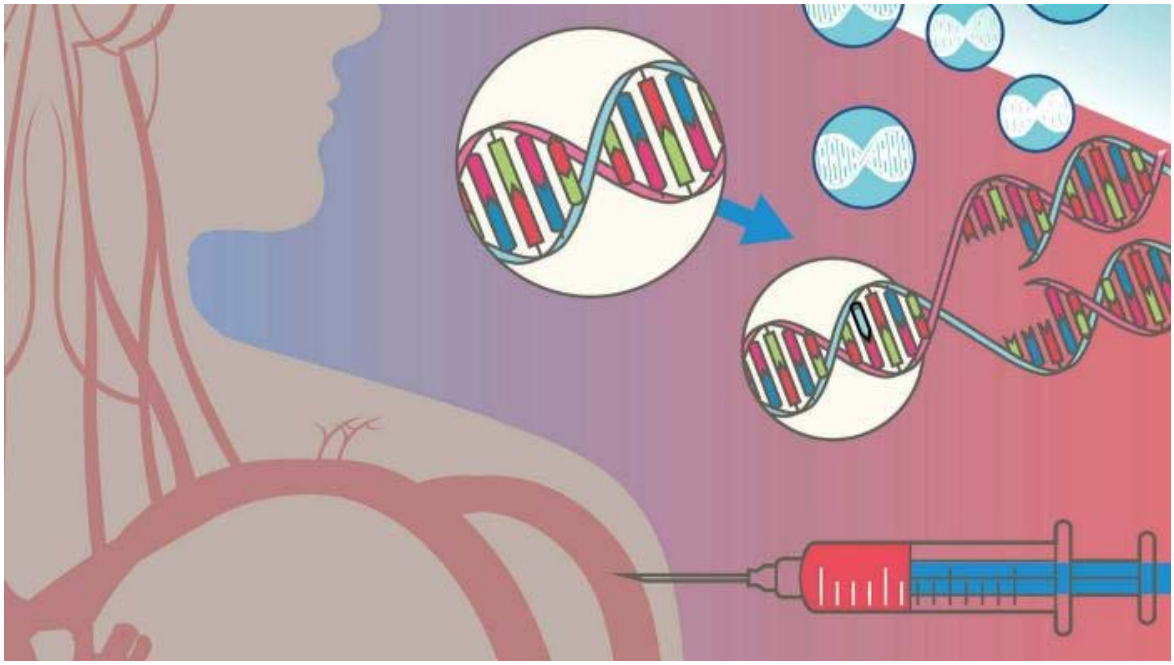
Coronavirus

Quest for accurate antibody tests in fight against Covid-19

Pinpointing who has developed resistance is vital for governments desperate to lift lockdown



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Clive Cookson, **Hannah Kuchler** and **Andrew Jack** YESTERDAY

Just a month ago the UK was promising what prime minister Boris Johnson called a "game changer" — the imminent roll out of millions of quick tests that would reveal who had been infected with coronavirus and developed antibodies to the disease.

But the plan for more than 3.5m at-home "pregnancy test" type kits to be distributed by retailers such as Boots and Amazon was scuppered when it was discovered that they were inaccurate.

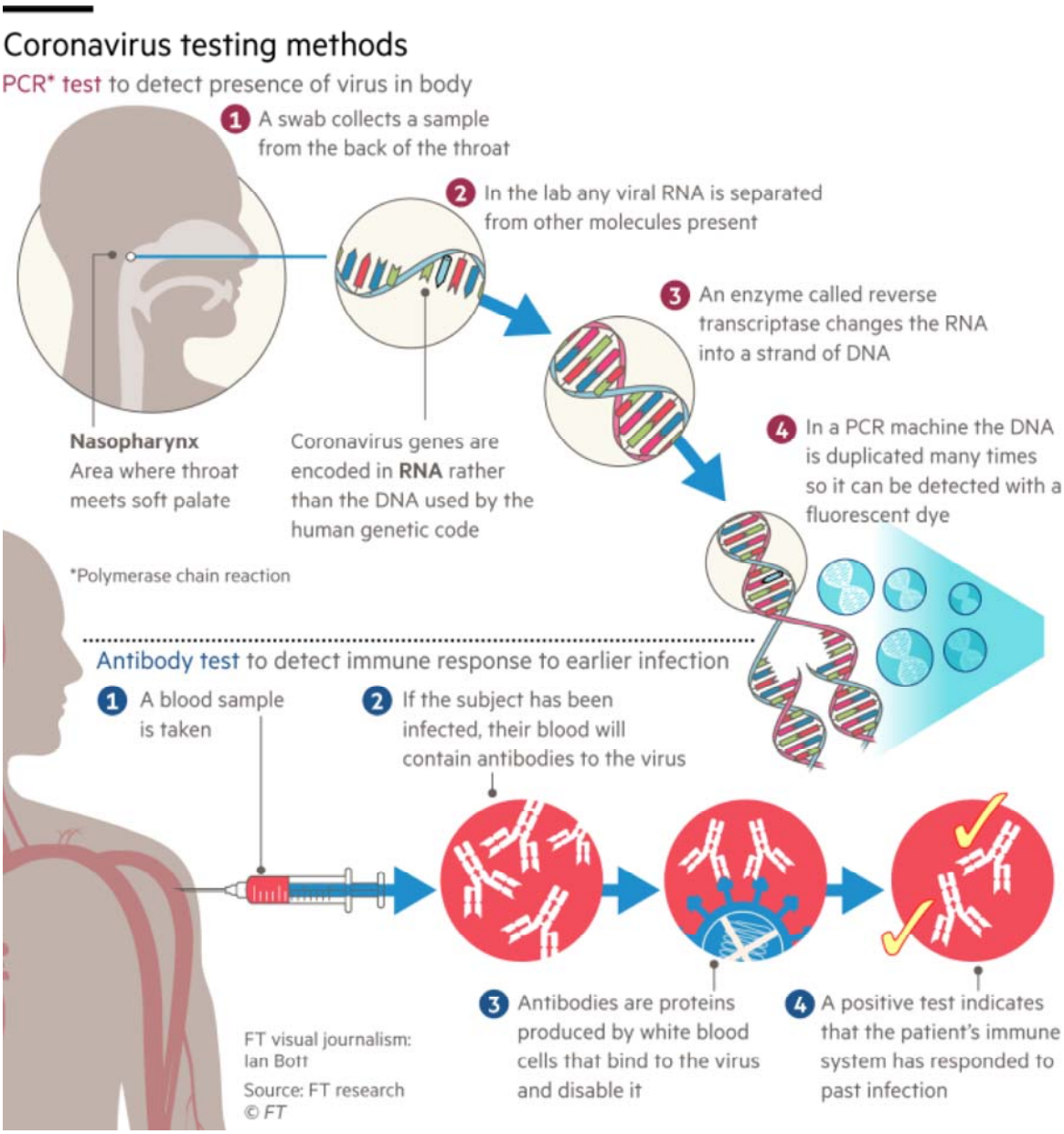
The National Covid Testing Scientific Advisory Panel in Oxford this week released the results of its evaluation of nine commercial antibody tests being considered by the UK government. None came close to meeting the required specifications for testing individuals for their immune response to Covid-19.

Simon Clarke, a microbiologist at the University of Reading, said the report "shows quite clearly that several different types of test kit were insufficiently accurate to be used by the general population and would in no way have been sufficient to determine whether people had been exposed to the coronavirus or if they were immune."

Antibody testing is seen as crucial in providing governments with the data to determine when it is safe to lift the lockdowns that have curtailed their citizens' personal lives and had a devastating effect on businesses and the global economy.

The tests should show whether individuals have acquired immunity from past infection, which would allow them to work and socialise without picking up the virus.

Testing large representative groups over a period of months or years would reveal the spread of infection and immunity in the population to inform vaccine development, epidemiological modelling and public health policy. It would answer one of the biggest questions about Covid-19: how strong and long-lasting the human response is.



The UK is not alone in experiencing difficulties with the tests, also known as serology tests, which analyse blood samples for specific antibodies produced by the human immune system to fight viral infection.

Problems have been reported worldwide, with Spain and other European countries rejecting large numbers of antibody tests imported from Asia, while the US Food and Drug Administration has been criticised for allowing dozens of companies to sell unvalidated tests of dubious quality.

Scott Becker, executive director of the Association of Public Health Laboratories in the US, said there had been a “flood” of more than 90 antibody tests on to the market, which were “frankly of dubious quality”.

Eric Topol, director of the Scripps Research Translational Institute, added: “Usually you can rely on the FDA to do due diligence and really make sure the test is valid but here the criteria have been loosened. If anything we need more oversight, rather than less.”

The global scramble for antibody tests has triggered a huge effort by biotech and diagnostics companies. The Foundation for Innovative New Diagnostics or Find, a non-profit organisation based in Geneva, lists 280 immunoassays (antibody tests) in development or on the market, many from Chinese companies.

Regulators in China recently cracked down on exporters that do not have certificates from Chinese authorities, after the test kits exported to Spain by Shenzhen Bioeasy Biotechnology turned out to have quality problems.

After returning the faulty Chinese kits, the Spanish government instead bought 20,000 antibody test kits from Sugentech, a South Korean company set up in 2011 by Sohn Mi-jin, who was leading diagnostics development for LG Life Sciences.

Sugentech began producing its Covid-19 antibody kits in early April after clinical trials in mid-March. It is exporting them to about 50 countries including the US and Europe and plans to ramp up production to about 2m tests a week in May.

“Although Chinese antibody kits are said to be only 30-50 per cent accurate, our products are more than 95 per cent accurate,” Mr Sohn claimed.

From this month Chinese enterprises that export Covid-19 detection reagents and other products must obtain a medical device registration certificate in China as well as meeting the quality standards of the importing countries. So far only 11 antibody test kits have received emergency approvals from the National Medical Products Agency.

“It is very easy to develop [antibody tests] but you have to validate them with enough patients,” said Severin Schwan, chief executive of Roche, the Swiss pharmaceutical company. “There are 150 companies producing them already, most from Asia,” he added. “I just get mad, it's so unethical . . . They are not only useless but can be damaging.”

However, the big diagnostics companies, including Roche and its US competitor Abbott, are now bringing their own serology tests to the market. They are designed to run on specialised equipment in hospitals and reference labs, which almost guarantees better results than the faster at-home or point-of-care tests that give a result within minutes by analysing a droplet of blood in a “lateral flow” device.

Developing an accurate test is a challenge because it must recognise antibodies specific to Sars-CoV-2, the virus responsible for Covid-19, without being distracted by similar antibodies that people may carry if they have been infected by related coronaviruses that circulate among people causing minor cold-like symptoms. It is much harder to diagnose past infection from the human antibodies Sars-CoV-2 generates than to detect current infection from its own distinct viral genes through PCR testing.

Scientists assess the accuracy of diagnostic tests in two ways. One is “specificity”, only recognising real cases and avoiding false positives. The other is “sensitivity”, identifying all real cases and avoiding false negatives.

The Oxford evaluation shows that commercial point-of-care tests do very well on specificity, picking up samples only from people who were really infected with Sars-CoV-2. Their weakness is sensitivity, failing to detect antibodies in about one-third of people who actually had them.

“This means if your test is positive, you can be confident that you have been infected and have antibodies,” explained Eleanor Riley, professor of immunology and infectious diseases at the University of Edinburgh. “But if your test is negative, you can’t rule out that you might have been infected.”

The good news from the Oxford study is that the lab test compared against the rapid point-of-care tests “showed excellent sensitivity and specificity,” said Prof Riley. “This means that public health labs now have a test that they can use to begin to understand what percentage of the general public have already been infected.”

Additional reporting by Camilla Hodgson, Jung-a Song and Xueqiao Wang