



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Analysis Antibody testing

The problems with so-called immunity tests

Initial antibody testing surveys suggest more people have been infected than we thought. But we need to be cautious about these results, reports **Michael Le Page**

ANTIBODY tests hold the promise of telling us how many people are already immune to the coronavirus. Unfortunately, serious issues with antibody testing mean we need to be very careful about how we use them.

So far, almost all coronavirus testing has looked for the presence of the virus in swabs of the nose or throat. But not every suspected case is tested in this way, so the actual number of cases in any country or region must be higher than official figures suggest.

The question is, how much higher? This matters because it can help indicate the best strategy for removing lockdowns and social distancing measures. In theory, tests that show how many people have antibodies against the coronavirus in their blood could tell us this.

Numerous research teams and companies worldwide are developing tests for antibodies, and some are already being used, but it is unclear how accurate most of them are, and few have undergone any kind of independent validation. The UK paid millions upfront for 2 million home antibody testing kits, as revealed mid-April by *The New York Times*,



VLADIMIR GERDOV/TASS VIA GETTY IMAGES

Blood is collected for antibody testing in a Moscow medical centre

before independent tests suggested the kits were unreliable.

But enthusiasm for antibody testing has remained high for two reasons: some kinds of antibody tests are easier to do than swab tests, and they may be able to tell us how many people are now immune to the coronavirus. This is a big may however – it isn't yet clear what role antibodies play in immunity to the coronavirus. On 24 April, the World

Health Organization released a statement saying that no study has yet "evaluated whether the presence of antibodies to [the virus] confers immunity to subsequent infection".

Nevertheless, many have begun to use antibody tests to try to get a picture of how many people have caught the coronavirus so far. The initial findings have been making headlines, even though many of these studies haven't been published yet, let alone peer-reviewed.

Some antibody surveys suggest that far more people have been infected than expected. For instance,

a study in Santa Clara county, California, where just 50 deaths have been attributed to the virus so far, claimed that up to 4 per cent of people there had been infected – up to 85 times the official figure – based on a survey of 3000 people (medRxiv, doi.org/dskd).

But the Santa Clara study and similar work elsewhere has come under fire. We should not be making policies based on studies that haven't been properly reviewed, says Daniel Larremore at the University of Colorado, Boulder. "It really matters that we get these things right."

There are two main issues with antibody surveys. The first is that when only a tiny percentage of a population has been infected, false positives can lead antibody testing to wildly overestimate the number of people who have encountered the virus.

The second is that it is hard to recruit and test a representative sample of the population, so results can end up being greatly skewed.

Beyond these issues, to refer to antibody testing as "immunity tests" is premature – we still don't know if it is possible to have covid-19 twice. ■

Vaccines

Trials of BCG vaccine will test for covid-19 protection

WHILE a coronavirus vaccine is still a way off, some believe we may have a stopgap in the BCG vaccine, which protects against tuberculosis (TB).

In countries with routine BCG vaccination, the pandemic appears to be less severe. This could be due to a long-standing but unproven hypothesis that the vaccine is a general immune-system enhancer.

The Max Planck Institute for Infection Biology in Berlin is

planning a clinical trial of a genetically modified version of BCG that has been shown to make mice more resistant to viruses like flu. The trial has regulatory approval and should start this week.

If it succeeds, millions of doses could be made available in a very short time, says Adar Poonawalla at the Serum Institute of India, a private company that is partnering with the Max Planck Institute to develop the vaccine. BCG trials have also begun in the Netherlands and Australia.

Some countries, including the US and Italy, have never had a national

BCG programme and others phased theirs out as TB became less of a concern – the UK stopped in 2005.

Gonzalo Otazu at the New York Institute of Technology has found that countries where the BCG vaccine is used have fewer covid-19 cases and/or deaths. He analysed the link using up-to-date information on worldwide BCG programmes.

"The correlation was very clear," he says. But he cautions that it is too

"BCG vaccination is a potential new tool in the fight against covid-19, but we have to wait for trials"

early to recommend action. "BCG vaccination is a potential new tool in the fight against covid-19, but we have to wait for the results of the ongoing clinical trials," he says.

Lone Graff Stensballe at the Danish National University Hospital is sceptical, both of the general immune-enhancing claims for BCG and the specific covid-19 idea.

"It has not been possible to detect such beneficial non-specific effects of BCG in well-designed studies," she says. "My advice would be to invest our scarce resources in other preventive measures." ■

Graham Lawton