

Ethical Aspects of COVID-19 Antibody Testing

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Abstract

One common COVID-19 test is the test for one or more of the antibodies the body creates when it encounters the COVID-19 virus. Because these tests are often Point-of-Care, rapid tests that require only a blood sample they may appear to patients as an easily accessible and useful tool for guiding their actions in the pandemic. However, serologic antibody tests should not be offered to patients in normal practice under nearly all circumstances. They are useful in narrow diagnostic settings in later stage infections and they serve an important public health function, but they are not of benefit to patients and may in fact give false and potentially harmful information to patients of moderate health literacy.

Introduction

A Point-of-Care, rapid serological test for antibodies to COVID-19 may appear to patients as an easily accessible and useful tool for guiding their actions in the pandemic. However, serologic antibody tests should not be offered to patients in normal practice under nearly all circumstances. It is not that the tests are inadequate at their role of detecting antibodies. The tests are helpful for knowing the spread of the virus, and so have an important public health role. They can also be an important diagnostic tool in late stage infections where the antibodies may be more easily detectable than the virus. Despite these valid uses, serologic antibody tests do not benefit patients and may unintentionally provide false and potentially harmful information to patients of moderate health literacy.

The controversy regarding COVID-19 antibody testing is that we do not know what the presence of antibodies means for a particular patient. There are four different types of tests: rapid detection tests (RDT), enzyme-linked immunosorbent assays (ELISA), Chemiluminescent immunoassay (CLIA), and neutralization assays. [1] RDT tests are point-of-care tests that give rapid results indicating only the presence or absence of antibodies, but no quantitative information; ELISA tests are tests that incubate samples with the viral protein to get an assessment of how many antibodies are present, usually in a laboratory setting and over the course of several hours. CLIA tests are also lab-based quantitative tests that can detect multiple types of antibody in a comparable time frame to the ELISA test. Neutralization assay tests would challenge the antibodies in the sample with live virus to see how well the antibodies would actually protect against reinfection (at least in vitro.) Since this would take days, would require at least a biosafety level 3 facility due to the use of live virus [1], and no neutralization assay tests are currently FDA approved, they will not be considered in this discussion. [2] In addition, for this discussion, it will be assumed that the tests have perfect specificity and sensitivity, which of course is never true; but since the tests will not be recommended anyway, the fact that they do not operate as accurately as assumed herein will simply make them even of less utility.

Framework for Bioethical Debate

A true positive result on an RDT, CLIA, or ELISA test means, for a given patient, either that they have had a prior infection or that they are currently infected. An RDT does not tell how many antibodies are present; none of the three types tells whether those anti-

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bodies are effective in preventing virus growth. Because of this, a positive antibody test gives no actionable information:

- It cannot be used to trace contacts, as the presence of antibodies does not tell us when the person was infectious.
- It does not tell us anything about whether the test subject is susceptible to future infection. See, e.g., the CDC Interim Guidance on serology “definitive data are lacking, and it remains uncertain whether individuals with antibodies (neutralizing or total) are protected against reinfection with COVID-19, and if so, what concentration of antibodies is needed to confer protection.” [3]
- It does not tell us whether the person is currently infected or infectious, or whether the infection was at some time in the past and the patient is now not contagious. See, e.g., the CDC “Limitations” in their testing guidelines: “Thus, serologic test results do not indicate with certainty the presence or absence of current or previous infection with COVID-19.” [3]

In addition to this lack of direct benefit, a moderately health-literate patient would likely assume that the presence of antibodies would indicate a prior (i.e., not currently active) infection, and protection against future infection. Since neither of these is necessarily true these assumptions could harm a patient who acts on them.

Consequently, the recommendations for a person after a positive antibody test are the same as after a negative antibody test or no test at all. *The CDC recommends (emphasis added):*

- Asymptomatic persons who test positive by serologic testing and who are without recent history of a COVID-19 compatible illness have a low likelihood of active infection and should *follow general recommendations* to prevent infection with COVID-19 and otherwise continue with normal activities, including work.
- Persons who have had a COVID-19-compatible or confirmed illness should *follow previous guidance* regarding resumption of normal activities, including work.
- There should be *no change* in clinical practice or use of personal protective equipment (PPE) by health care workers and first responders who test positive for COVID-19 antibody. [3]

Or, to put it another way, a positive test result means you must approach COVID-19, and its potential to infect you and others, just as you would have prior to the antibody test. And if a test comes back negative, you would follow, again, exactly these same guidelines.

A useful comparison may be drawn here to a more commonly known circumstance. A 25-year-old male presenting in primary care with possible appendicitis with an Alvarado score ≥ 7 or an AIM score ≥ 9 should not be sent for a CT scan, or even the less expensive ultrasound. [4] While both of these are highly accurate tests, the results will not actually be helpful. The Alvarado and AIM scores are obtained by clinical findings and shown to indicate a high (87 to 88%) likelihood of appendicitis. Consequently, even if a CT scan or ultrasound came back with uncertain or negative results the recommendation should still be to send them to the ER for immediate surgical evaluation, as even a short delay in diagnosis and treatment greatly increases the risk of perforation and sepsis. A positive result would also indicate sending the patient to the ER; so even though a CT or ultrasound are accurate diagnostic tools they do not provide information that should lead to different actions. Consequently, in normal practice CT and ultrasound are not recommended in primary care when the clinical findings are so significant for indicating appendicitis. [4]

A positive antibody test will have the following results:

1. It will confirm a probable infection with COVID-19 at some time in the past, or a still active infection.
2. It may imply to a moderately health-literate test subject that they are not currently infected with, and are immune to reinfection with, COVID-19 (which may not be true.)

A negative antibody test will have the following results:

1. It will indicate either that a patient has not been infected with COVID-19 or that they are currently infected but have not yet developed detectable antibodies.
2. It may imply to a moderately health-literate test subject that they are not currently infected with COVID-19 (which may not be true.)

And in either case:

3. It will make no difference in the recommendations you make to a patient who is currently not suffering from any effects of a COVID-like illness.
4. It will make no difference in the recommendations you make to a patient who is currently suffering from effects of a COVID-like illness.

Even assuming perfect specificity and sensitivity, the results of an antibody test will have no accurate positive impacts and will have potential negative impacts through potentially misleading patients.

The pillars of bioethics apply to this unfortunate dynamic clearly:

1. **Beneficence** (act in a patient's best interest): is testing in the patient's best interest, or is testing in the interest of public health, science, and the science perfecting COVID antibody testing? Though COVID-19 antibody testing may benefit society and the patient eventually through the data in bio-samples, this benefit to a patient is very low and carries with it the risks noted herein.
2. **Non-Maleficence** (do no harm): are we ensuring that taking people's blood samples is done without harm to the patient? Since a patient might be harmed by misunderstanding the implications of the results of the test and will gain very little of note from those results, it is likely that the harm to the patient will outweigh the benefits. In addition to concerns about harms via accidental misinformation that a patient may infer, there are concerns of privacy common to biorepositories, including who has custody of the samples, where the biorepository of samples will be, and what will be done with the samples besides antibody testing, such as genetic testing.
3. **Autonomy** (respect the patient's informed choices): Is it possible to communicate adequately to many patients that as of now, the antibody tests may not yield the information they think it yields? In particular, since the concept of antibodies producing resistance to viral infections is the basis of vaccines that the general public generally recognizes, it may be very difficult and time-consuming to explain that this is not known in the case of COVID-19. This may become easier as news stories regarding the issue enter the public conscious, but at the moment this is a major challenge to accurately informing patients. [5]

Exceptions in Support of Testing

There is a positive rationale for doing antibody testing in two restricted areas, neither of which are of the type discussed above.

First, an antibody test can be used in a symptomatic person suspected to be in the later stages of a COVID-19 infection as a diagnostic tool. [3] In later stages of infection (approximately 9-14 days after the onset of illness) testing for viral presence can be unclear, as the virus may not be present in significant amounts. If antibodies are present, that indicates a likelihood that the infection is a COVID-19 infection.

The second is a public health/epidemiology reason: presumably, these tests give a good indication of how widespread the infection has been in a population. This can give an after the fact analysis of how widespread asymptomatic infections were, which would give more information about how deadly the virus is, how far it has spread, and how effective contact tracing might be in future waves.

These are valid reasons for doing antibody testing, but these do not significantly benefit the individual being tested. So as arguments for providing testing to persons concerned about their current or prior infection status, these do not work well.

Conclusion

Despite the perceived value to patients of knowing whether they have been previously exposed to and infected by COVID-19, RDT, ELISA, and CLIA serologic antibody tests ought not be offered or provided in normal practice outside of the exceptions noted above, as they lead to no actionable patient knowledge and may lead to dangerous misinformation.

Appendix: CERID COVID-19 Study Group

Available upon request.

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