**Tests for antibodies against SARS CoV2**. July 2020[1].

*Taking forward a recommendation from SAGE45 to the Senior Clinicians Group, 7th July 2020*

**Summary question:**

In the light of recent findings presented to SAGE and their request to the senior clinicians' group, should a testing strategy be developed including antibody, swab testing and Ct determination to enable earlier release from quarantine/isolation?

**Issues to discuss:**

1. The Barclay/Openshaw paper to SAGE on 2nd July addressed the questions: is someone with antibodies likely to be able to still transmit the virus without becoming symptomatic themselves; what information do antibody tests provide towards this and how reliable are these tests particularly those commercially available?

2. The authors' conclusions are that:
    a. It is reasonable to assume that people with antibodies are less likely to be infected, albeit their degree of protection (particularly in the longer term) is unclear. Some may have supressed symptoms and localised infection (e.g. nasal).
    b. Virus transmission can take place from pre-symptomatic and asymptomatic individuals if they have sufficient replicating virus in the nose, lungs or throat. This is an increasingly common conclusion of UK studies.
    c. It is unlikely that people recovering from SARS-CoV-2 infection who have developed antibodies in the nasal secretions, blood or serum are still infectious. However, this has not been formally proven.
    d. This is concluded because some people who are recovering from infection may have viral RNA (detected by the swab PCR test on a nasal swab); but do not shed live virus that can be grown in a lab or infect others. The loss of viral infectivity happens at about day 8-14 when the viral load (detected by PCR) is in decline and antibody is starting to appear[2].

3. This has led SAGE to conclude with medium confidence that*, although immunity from neutralising antibodies after three months is uncertain, in the short term, individuals who are both antibody positive and PCR positive are much less likely to be infectious. This offers a way forward in releasing people earlier from self-isolation and quarantine.*

    *Furthermore, in conjunction with the Barclay/Openshaw conclusions, an industry standard is needed for the hundreds of commercial antibody tests available whose quality is variable but whose sensitivity and specificity are improving. Immunity passport introduction would be premature.*

[1] **Tests for antibodies against SARS CoV2**. July 2020. Wendy Barclay and Peter Openshaw. Presented to SAGE45, 2nd July 2020

[2] MEDRXIV-2020-125310v1-vanKampen, *reference presented in the Barclay/Openshaw paper*.

## 4. Preamble and questions for the clinicians' group:

4.1. [Preamble] *The questions are posed in the context of releasing anybody from isolation or quarantine. Do clinicians agree?*

4.2. In the light of loss of viral infectivity at about day 8-14 when the viral load (detected by PCR) is in decline and antibody is starting to appear, is there merit in testing on day 8 for: PCR, antibody and Ct values to enable earlier release from quarantine?

**4.**2. Would clinicians agree that this applies to those who were symptomatic and (where known) asymptomatic on initial PCR testing?

4.3. Given the caution about quality and interpretation of commercial tests, should clinicians determine an agreed reliable antibody test for common use for the purpose of release from quarantine?

4.4. Can the system adequately address this combination of testing and who should be responsible for such testing?

Yvonne Doyle
5th July 2020.

## 5. Outcome of the discussion with senior clinicians.

5.1. Senior clinicians were unanimous that the proposal to test in this manner was not justified at this time. The approach was considered complex and posed the risk of contradicting the clear current message that isolation and quarantine is necessary to control the spread of the virus. It could also lead to gaming the system to get early release.

5.2. Research under way on testing large populations in the UK will inform us further about immunity so clinicians did not rule out a re-look at this combination of testing in the future.

Yvonne Doyle
8th July 2020

## Appendix 1. Key conclusions of Barclay and Openshaw

**Are antibody tests able to provide information on a person's immunity?**

Tests that measure antibodies to RBD might be a correlate of immunity, but

a) we don't yet know what levels of such antibodies are required for protection,
b) we don't know for certain that protection can be conferred by neutralizing antibody in humans, as opposed to animal models, because there has not been a human challenge either in an experiment or during a known natural re-exposure.

**Is someone with antibodies likely to be able to still transmit the virus without becoming symptomatic themselves?**

It is reasonable to assume that people with antibodies are less likely to be infected, but we at present do not know how much protection is conferred by an immune response, and for how long. It is possible that those with antibody can be infected and that symptoms might be supressed despite localised infection (i.e. in the nose).

Virus transmission can take place from presymptomatic and asymptomatic individuals. Therefore, people without symptoms can still infect others if they have sufficient replicating virus in the nose, lungs or throat.

However, some people who are recovering from infection may have viral RNA (detected by the swab PCR test on a nasal swab) but do not shed live virus that can be grown in a lab or infect others. The loss of viral infectivity happens at about day 8-14 when the viral load (detected by PCR) is in decline and antibody is starting to appear (MEDRXIV-2020-125310v1-vanKampen).

**It is unlikely that people recovering from SARS-CoV-2 infection and have developed antibody in the nasal secretions, blood or serum are still infectious.** However, this has not been formally proven.

**Commercial tests for antibodies to SARS CoV2**

In conclusion, although early reports suggested poor performance that would preclude utility, some of the commercial tests that have come to market more recently are performing well.

**At present there is insufficient evidence that knowledge of an individual's immune status can be relied upon to enable a change in behaviour. This is because the tests themselves have lower than ideal specificity, and we do not yet know that a positive results in such a test guarantees protective immunity.**