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Humoral response and PCR positivity in patients with COVID-19 in the New York City region, USA: an observational study

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Summary

Background Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic. The proportion of infected individuals who seroconvert is still an open question. In addition, it has been shown in some individuals that viral genome can be detected up to 3 months after symptom resolution. We investigated both seroconversion and PCR positivity in a large cohort of convalescent serum donors in the New York City (NY, USA) region.

Methods In this observational study, we ran an outreach programme in the New York City area. We recruited participants via the REDCap (Vanderbilt University, Nashville, TN, USA) online survey response. Individuals with confirmed or suspected SARS-CoV-2 infection were screened via PCR for presence of viral genome and via ELISA for presence of anti-SARS-CoV-2 spike antibodies. One-way ANOVA and Fisher’s exact test were used to measure the association of age, gender, symptom duration, and days from symptom onset and resolution with positive antibody results.

Findings Between March 26 and April 10, 2020, we measured SARS-CoV-2 antibody titres in 1343 people. Of the 624 participants with confirmed SARS-CoV-2 infection who had serologies done after 4 weeks, all but three seroconverted to the SARS-CoV-2 spike protein, whereas 269 (37%) of 719 participants with suspected SARS-CoV-2 infection seroconverted. PCR positivity was detected up to 28 days from symptom resolution.

Interpretation Most patients with confirmed COVID-19 seroconvert, potentially providing immunity to reinfection. We also report that in a large proportion of individuals, viral genome can be detected via PCR in the upper respiratory tract for weeks after symptom resolution, but it is unclear whether this signal represents infectious virus. Analysis of our large cohort suggests that most patients with mild COVID-19 seroconvert 4 weeks after illness, and raises questions about the use of PCR to clear positive individuals.

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Introduction Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19, has rapidly spread around the world, leading to unprecedented strain on health-care systems and economies and causing more than 405 000 infections and 25 000 deaths in New York State (New York State, Department of Health, NYSDOH COVID-19 tracker) as of July 20, 2020. Substantial disruptions to daily life have been enacted to flatten the epidemic curve. To avoid spread of SARS-CoV-2 and to help standardise definitions of clearance, it is important to understand the duration of SARS-CoV-2 nucleic acids within the nasopharynx and the time course to the mounting of an antibody response to this new viral pathogen.

Current US Centers for Disease Control and Prevention (CDC) guidelines suggest that people with confirmed or suspected SARS-CoV-2 infection should remain in isolation for at least 10 days from symptom onset and return to work if they have been asymptomatic for at least 72 h. However, so far, there are limited data that help to define the time to viral clearance from illness onset and cessation of symptoms. A previous case study suggested that SARS-CoV-2 can exhibit ongoing viral shedding for a median of 2–5 days (range 1·0–8·0) after complete symptom resolution, but it remains unclear whether this viral shedding poses a risk for forward transmission.1 A small case sample of four patients admitted to hospital were SARS-CoV-2 positive on repeat RT-PCR testing 5–13 days after discharge.2 Other studies have found viral shedding for up to 3 months after symptoms resolve.3 From work with the 2003 SARS-CoV, it is not clear whether detection of viral genome of this duration indicates prolonged infectivity or the presence of
Research in context

Evidence before this study
We searched PubMed, medRxiv, and bioRxiv for research articles and preprints published in English between Jan 1 and May 1, 2020, using the terms “SARS CoV 2”, “Covid 19”, “ELISA antibody”, and “PCR”. We did not find reports of ELISA antibody assays as large as this one from areas with major COVID-19 hotspots, and found mixed and growing reports of IgG response to and PCR positivity for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) over time.

Added value of this study
We report on a large cohort of patients who recovered from mild COVID-19, and our findings show that the majority of patients with PCR-confirmed SARS-CoV-2 infection have an IgG response. More than a third of patients without PCR-confirmed SARS-CoV-2 had positive IgG, and a significant minority of patients had positive PCR results despite full resolution of symptoms for more than 2 weeks.

Implications of all the available evidence
Our findings suggest that IgG antibodies develop over a period of 7–50 days from symptom onset and 5–49 from symptom resolution, suggesting that the optimal timeframe for widespread antibody testing is at least 3–4 weeks after symptom onset and at least 2 weeks after symptom resolution. We also present the common finding of persistent PCR positivity, which raises issues regarding use of PCR testing for clearance of disease. Both of these findings have policy implications as the pandemic continues to spread around the world.

| All (n=624) | Positive for antibodies (n=211) | Weakly positive for antibodies (n=42) | Negative for antibodies (n=71) | p value |
|--------------|----------------------------------|-------------------------------------|--------------------------------|---------|
| Age, years   | 39·14 (12·09; 17–76)             | 39·11 (11·94; 17–76)                | 38·10 (12·28; 18–67)           | 40·00 (13·19; 19–74) | 0·71   |
| Age by category, years | ... | ... | ... | ... | ... |
| 17–29        | 144 (23%)                        | 110 (22%)                          | 15 (36%)                       | 19 (27%) | ... |
| 30–59        | 432 (69%)                        | 364 (71%)                          | 24 (57%)                       | 44 (62%) | ... |
| ≥60          | 48 (8%)                          | 37 (7%)                            | 3 (7%)                         | 8 (11%)  | ... |
| Gender       | ...                              | ...                                | ...                            | ...      | 0·0015 |
| Male         | 368 (59%)                        | 303 (60%)                          | 33 (81%)                       | 32 (46%) | ... |
| Female       | 252 (41%)                        | 206 (40%)                          | 8 (19%)                        | 38 (54%) | ... |
| Test results | All still PCR positive at next test | 217 (35%) | 159 (31%) | 22 (52%) | 36 (51%) | NA |
| Time from last positive PCR to current result, days | 22 (18–27) | 22 (18–28) | 19 (16–27) | 20 (16–26) | 0·0001 |
| Symptoms, days | ...                              | ...                                | ...                            | ...      | ... |
| Onset to result | 23 (20–26) | 23 (20–27) | 20 (18–22) | 21 (17–25) | <0·0001 |
| Resolution to result | 14 (11–17) | 14 (11–17) | 14 (10–16) | 12 (9–15) | 0·010 |
| Symptom duration | 9 (6–12) | 9 (6–12) | 7 (4–10) | 10 (4–15) | 0·030 |

Table I: Respondents with past PCR-confirmed COVID-19

non-viable virus. A clearer understanding of the duration of viral shedding is crucial for preventing transmission by infected individuals, particularly as they begin to feel well enough to resume normal activities. An understanding of the time to PCR clearance might also help to guide isolation durations and return to work clearance, as well as clarify the usefulness of negative PCR testing as part of defining disease clearance.

There are limited data worldwide on the development of antibodies against SARS-CoV-2, particularly the formation of IgG. There is concern regarding efficacy of antibody testing for diagnosis of SARS-CoV-2, and little is known about long-lasting immunity. One study measured neutralising antibodies in 175 patients admitted to hospital and found that 64% had high antibody titres, 30% had weak antibody response, and 6% had undetectable titres. Studying the plasma from previously infected individuals might improve our understanding of the timing and strength of different populations’ antibody response to this novel illness, delineate the duration of antibody presence, and identify cases of possible reinfection. Additionally, individuals with high antibody titres might become donors for convalescent plasma treatment for patients who are critically ill as part of ongoing studies of this therapeutic option.

We present a large dataset of serum antibody testing completed at Mount Sinai Hospital (New York, NY, USA) in people who have fully recovered after mild illness from SARS-CoV-2 infection. We aimed to describe the time to SARS-CoV-2 PCR clearance from the nasopharynx, the rates of IgG development, and time to serum IgG development from onset and resolution of symptoms in participants with previously confirmed or suspected SARS-CoV-2 infection.

Methods
Study design and participants
In this observational study, we ran an outreach programme in the New York City (NY, USA) area, including parts of Connecticut and New Jersey, to identify people who had recovered from SARS-CoV-2 infection for nasopharyngeal PCR (cobas 6800; Roche Diagnostics, Indianapolis, IN, USA) and serum IgG titre measurement (ELISA; Icahn School of Medicine at Mount Sinai, New York, NY, USA). We recruited participants via the REDCap (Vanderbilt University, Nashville, TN, USA) online survey response, which was advertised on our hospital website, and subsequently shared by several news organisations and public officials in New York. REDCap respondents were deemed to be eligible if they had previously tested positive.
for SARS-CoV-2 or if they were symptomatic with suspected SARS-CoV-2 and in a high-risk group. Sympto-
matic individuals deemed to be at high risk were those
who either lived with someone with a positive SARS-CoV-2
PCR test, had been told by a physician that they had
symptoms consistent with SARS-CoV-2, or were health-
care workers. We only included participants who self-
reported suspicious symptoms after Feb 1, 2020, as
SARS-CoV-2 is believed to have begun to spread in New
York City from this time. Additionally, only participants
who were asymptomatic at the time of survey were
contacted. Respondents self-reported date of symptom
onset, date of positive SARS-CoV-2 test (if applicable), and
last date of symptoms. Duration of symptoms was
 calculated from these self-reported dates. This study was
reviewed and approved by our institutional review board.

**Viral PCR**

During the first 2 weeks of the survey, we tested for
SARS-CoV-2 in the nasopharynx by PCR as well as IgG
antibody in the serum of every individual, whereas in the
third week the testing was limited to SARS-CoV-2 antibo-
dies only. The rationale for this change was that more
data are available on lack of infectiousness with symptom
resolution more than 14 days before testing. During
week 1, participants were brought in 10 days after they had
a confirmed or suspected diagnosis and had been asympto-
matic for at least 3 days. In week 2, as we identified more
potential donors and learned more about our antibody
assay, we extended our timeline to 14 days after symptom
onset, with at least 3 days asymptomatic. In week 3, we
included participants 21 days or more after symptom
onset, who had been completely asymptomatic for at least
14 days.

SARS-CoV-2 PCR was considered to be positive if
detected on nasopharyngeal swab. A close agreement has
been shown between the cobas 6800 used in this study and
two other widely implemented SARS-CoV-2 PCR tests:
Cepheid GeneXpert (Cepheid, Sunnyvale, CA, USA) and
Hologic Panther Fusion (Hologic, Marlborough, MA,
USA).12–14

**SARS-CoV-2 IgG**

We measured serum IgG antibody titres using a
serological ELISA developed at Icahn School of Medicine
at Mount Sinai and described on March 18, 2020; this
serum test has a sensitivity of 92% and a specificity of
more than 99% as per our US Food and Drug
Administration (FDA) emergency use authorisation.15
Increasing titres in the Mount Sinai ELISA assay have
been shown to correlate with viral neutralisation.16 Serum IgG antibody titres were considered to be strongly positive if they were detected at titres of 1:320 or higher (highest dilutions were 1:320, 1:960, and 1:2880), and considered to be weakly positive if detected at titres of 1:80 and 1:160. As per the FDA emergency use authorisation, detected means that a sample was above the optical density cutoff of 0.15 in the receptor binding domain screening ELISA and had a titre of at least 1:80 in the spike confirmatory titration. Negative was defined as titres below 1:80 (and is shown in figures as 1:40 for representation purposes). All interested participants with antibody titres of more than 1:320 and negative SARS-CoV-2 PCR swabs were screened by the New York Blood Center using standard criteria for plasma donation and included as donors in our convalescent plasma study if eligible. Participants with weakly positive antibody titres were invited to return for repeat serum titre testing at least 7 days after their initial antibody test. Participants with positive PCR swabs and antibodies were asked to return for PCR testing at least 3 days after initial PCR test so they could be referred for plasma donation once the virus had fully cleared.

Figure 1: Antibody responses in individuals with PCR-confirmed COVID-19
(A) Antibody testing results days after symptom onset stratified into titre
categories. A longer interval between symptom onset and testing usually leads to
titres at higher titres. The highest titre category contains both 1:2880 and more than
1:2880 titres. Bars represent the mean, and error bars represent the SD.
(B) Individuals with negative titres were recalled for retesting. Both the original
test result and the second test result after the day of onset are shown. Negative
titres were assigned a value of 1:40 for representation purposes; the dashed line
represents the cutoff between positive and negative titres. Only results for
individuals for whom date of symptom onset is known are shown.
Articles

Viral genome was detected in nasopharyngeal swabs of individuals screened as plasma donors. Numbers of PCR results of individuals with initially PCR-confirmed COVID-19 were shown. More than one result from an individual might be shown if tested more than once on different days. Only results for individuals for whom a date of symptom resolution was available are shown.

Figure 2: PCR results of individuals with initially PCR-confirmed COVID-19

Viral genome was detected in nasopharyngeal swabs of individuals screened as plasma donors. Numbers of PCR results of individuals with initially PCR-confirmed COVID-19 were shown. More than one result from an individual might be shown if tested more than once on different days. Only results for individuals for whom a date of symptom resolution was available are shown.

Results

Between March 26 and April 10, 2020, we measured SARS-CoV-2 antibody titres in 1343 people. The mean age of the participants was 40·35 years (SD 12·18) with 256 (19%) participants aged 17–29 years, 968 (72%) aged 30–59 years, and 119 (9%) aged 60 years or older. 706 (53%) participants were male and 624 (46%) had confirmed SARS-CoV-2 diagnosis by previous PCR testing. The median number of days between symptom onset to serum antibody test was 24 (IQR 21–28), the median number of days between symptom resolution to antibody test was 15 (12–20), and median duration of symptoms was 9 days (6–13). Of the 1343 participants, 18 (1%) were referred to our REDCap after an emergency room visit or admission to hospital in the Mount Sinai Hospital system; the other 1325 (99%) were self-referral individuals who had mild to moderate symptoms.

In the 584 participants for whom both nasopharyngeal PCR testing and serum antibody testing was available, SARS-CoV-2 RNA was detected in 249 (43%) at a median of 20 days (IQR 18–23) from symptom onset and 12 days (9–14) from symptom resolution.

624 participants had confirmed SARS-CoV-2 disease by PCR before coming for testing; 606 (97%) were by self-report and 18 (3%) were documented in our electronic medical record. If self-reported, participants provided the date of testing. In this subgroup, the mean age was 39·14 years (SD 12·09) and 368 (59%) participants were male (table 1). At first test, 511 (82%) were strongly antibody positive at a titre of 1:320 or more, 42 (7%) were weakly positive, and 71 (11%) were negative (figure 1A). We asked 113 (18%) of 624 participants with an initial negative or weakly positive antibody response to return for a second test 10 or more days later. At the time of the first test, 217 (35%) were still PCR positive (range 5–22 days from symptom onset); figure 2). Median duration of symptoms in this group was 9 days (IQR 6–13). Age was not associated with a strong antibody response (p=0·17), whereas male gender was associated with a stronger response (p=0·0015). Longer duration between symptom onset and antibody test was associated with a higher titre antibody test (median 23 days [IQR 20–27] for positive titre vs 20 days [18–22] for weakly positive, p<0·0001; table 1). Symptom duration was also associated with higher antibody titres (median 9 days [IQR 6–12] for positive titre vs 7 days [4–10] for weakly positive, p=0·030; table 1). This finding can also be clearly observed in figure 1A, which plots titres against days after symptom onset.

In the subgroup of 719 participants with suspected disease who did not have confirmed SARS-CoV-2 infection, mean age was 41·39 years (SD 12·16) and 338 (47%) were male (table 2). 250 (35%) were strongly antibody positive, 19 (3%) were weakly positive, and 436 (62%) were negative at the first test. Antibodies were measured a median of 32 days (IQR 28–38) from symptom onset and 23 days (18–29) from date of symptom resolution. In this group, younger age was

Table 2: Respondents with suspected COVID-19, not confirmed by PCR

| Age, years | All (n=719) | Positive for antibodies (n=250) | Weakly positive for antibodies (n=19) | Negative for antibodies (n=450) | p value |
|-----------|------------|--------------------------------|--------------------------------------|--------------------------------|---------|
| Age by category, years | - | - | - | - | 0·0093 |
| 17–29 | 112 (16%) | 55 (22%) | 4 (21%) | 53 (12%) | - |
| 30–59 | 536 (75%) | 174 (70%) | 12 (63%) | 350 (78%) | - |
| ≥60 | 71 (10%) | 21 (8%) | 3 (16%) | 47 (10%) | - |
| Gender | - | - | - | - | 0·36 |
| Male | 318 (47%) | 123 (49%) | 11 (58%) | 204 (45%) | - |
| Female | 381 (53%) | 127 (51%) | 8 (42%) | 246 (55%) | - |
| Live with someone who tested positive | 62 (9%) | 33 (13%) | 1 (5%) | 28 (6%) | 0·064 |
| Had direct patient contact | 69 (10%) | 24 (10%) | 1 (5%) | 44 (10%) | - |
| Told by doctor had COVID-19 | 264 (32%) | 115 (46%) | 10 (53%) | 139 (31%) | - |
| p value | 0·0056 |
| Symptoms, days | - | - | - | - | - |
| Onset to result | 28 (25–26) | 26 (24–29) | 26 (24–28) | 32 (27–44) | <0·0001 |
| Resolution to result | 19 (15–21) | 18 (15–20) | 17 (13–23) | 22 (17–36) | <0·0001 |
| Symptom duration | 10 (6–14) | 8 (6–11) | 11 (6–14) | 10 (7–15) | 0·0032 |

Data are mean (SD; range), n (%), or median (IQR).
associated with stronger antibody response (p=0·0071). Gender was not significantly associated with antibody response in this group (p=0·36; table 2).

Of the 113 participants with PCR-confirmed SARS-CoV-2 infection and weakly positive or negative titres on their first serum antibody test, 64 have returned for follow-up antibody titres as of May 1, 2020. Of these participants, 57 (89%) displayed increased titres between the two tests, and three (5%) remained negative. The three that remained negative all self-reported positive PCR testing (none was available (only three values available). Of the 13 patients with PCR-confirmed SARS-CoV-2 infection and weakly positive or negative titres on their first serum antibody test, 64 have returned for follow-up antibody titres as of May 1, 2020. Of these participants, 57 (89%) displayed increased titres between the two tests, and three (5%) remained negative. The three that remained negative all self-reported positive PCR testing (none was available (only three values available).

Although all 1343 survey participants self-reported complete resolution of symptoms before testing, 249 (19%) tested positive for nasopharyngeal SARS-CoV-2 RNA. The maximum time of positive nasopharyngeal PCR testing was 43 days from symptom onset and 34 days from symptom resolution. For the 182 individuals who returned for repeat nasopharyngeal swabbing at least 3 days after a previous positive test, 112 (62%) were negative on the repeat test, a median of 10 days (IQR 7–12) after the first test. 70 (38%) remained positive and were rescheduled for another nasopharyngeal PCR 7–10 days later (table 4).

### Table 3: Participants (n=64) with second antibody test as of April 24, 2020

| Antibody result          | Test 1* | Test 2† |
|--------------------------|---------|---------|
| Positive                 | 0       | 48 (75%)|
| Weakly positive          | 19 (30%)| 13 (20%)|
| Negative                 | 45 (70%)| 3 (5%)  |
| Time between results 1 and 2, days | 13 (11–17) | –     |

| Change in result          |         |         |
|--------------------------|---------|---------|
| Negative to positive      | –       | 33 (52%)|
| Negative to weakly positive| –      | 9 (14%) |
| Negative to negative      | –       | 3 (5%)  |
| Weak positive to positive | –       | 15 (23%)|
| Weak positive to negative | –       | 0       |
| Weak positive to weak positive| –     | 4 (6%)  |
| Time between results by result change, days |         |         |
| Negative to positive      | 14 (11–20) | –       |
| Negative to weakly positive| 12 (13–15)| –       |
| Negative to negative      | 14 (12–15)| –       |
| Weak positive to positive | 11 (10–13)| –       |
| Weak positive to negative | –       | –       |
| Weak positive to weak positive| 15 (13–18)| –   |

| Symptoms, days            |         |         |
|--------------------------|---------|---------|
| Onset to result           | 19 (16–21)| 32 (28–33)|
| Resolution to result      | 12 (9–14)| 24 (21–28)|
| Symptom duration          | 5 (3–11) | –       |

Data are n (%) or median (IQR) unless otherwise stated. *First test restricted to April 10, 2020, or earlier. †Second test on April 22, 2020, or earlier. ‡Two (3%) patients had a third positive antibody test. §Change given because no IQR was available (only three values available).

### Table 4: Participants (n=182) with second PCR test as of April 24, 2020

| PCR result                  | Test 1* | Test 2† |
|-----------------------------|---------|---------|
| Detected†                   | 182 (100%)| 70 (38%)|
| Not detected§               | –       | 112 (62%)|
| Time between results 1 and 2, days | 10 (7–12) | –       |

| Change in result            |         |         |
|-----------------------------|---------|---------|
| Detected to detected        | –       | 70 (38%)|
| Detected to not detected    | –       | 112 (62%)|
| Time between results by result change, days |         |         |
| Detected to detected        | 10 (7–11)| –       |
| Detected to not detected    | 10 (7–13)| –       |

| Symptoms, days              |         |         |
|-----------------------------|---------|---------|
| Onset to result             | 20 (18–23)| 30 (26–33)|
| Resolution to result        | 12 (9–14)| 22 (18–26)|
| Symptom duration            | 8 (5–11) | –       |

Data are n (%) or median (IQR). SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *First test restricted to April 10, 2020, or earlier. †Second test on April 22, 2020, or earlier. §Eight patients had a third test in which SARS-CoV-2 was detected. Six patients had a third test in which SARS-CoV-2 was not detected.

Discussion

Our survey provides a large cross-sectional representation of SARS-CoV-2 RNA and antibodies found in participants recruited after recovery from SARS-CoV-2 during the early weeks of the outbreak in the New York City region. An understanding of the duration of potential infectiousness and the time to IgG antibody response is crucial to the containment of SARS-CoV-2 and the plans for widespread antibody testing over the coming months. Some countries, states, and organisations might even be considering antibody testing before letting individuals return to work.

In contrast to some of the previous literature on formation of antibodies, more than 99% of the patients who self-reported or had laboratory-documented SARS-CoV-2 infection developed IgG antibodies using our assay. Additionally, our findings suggest that IgG antibodies develop over a period of 7–50 days from SARS-CoV-2 infection and weakly positive or negative titres on their first serum antibody test, 64 have returned for follow-up antibody titres as of May 1, 2020. Of these participants, 57 (89%) displayed increased titres between the two tests, and three (5%) remained negative. The three that remained negative all self-reported positive PCR testing (none was documented in our electronic medical record; table 3).

Although all 1343 survey participants self-reported complete resolution of symptoms before testing, 249 (19%) tested positive for nasopharyngeal SARS-CoV-2 RNA. The maximum time of positive nasopharyngeal PCR testing was 43 days from symptom onset and 34 days from symptom resolution. For the 182 individuals who returned for repeat nasopharyngeal swabbing at least 3 days after a previous positive test, 112 (62%) were negative on the repeat test, a median of 10 days (IQR 7–12) after the first test. 70 (38%) remained positive and were rescheduled for another nasopharyngeal PCR 7–10 days later (table 4).

Although we do not yet know what, if any, immunity is conferred by IgG or the duration of the IgG response, at this time it seems likely that IgG against SARS-CoV-2 might confer some level of immunity based on what is
known about viral immunity to other pathogens. In previous studies of patients with SARS-CoV and MERS-CoV infection, IgG peaked within months of primary infection and waned over time.\(^5\)–\(^9\) Similar observations have been made with human coronaviruses, whereby immunity can confer at least limited protection.\(^9\)

To study the duration of IgG antibody response to SARS-CoV-2, we plan to follow our cohort for the next 6 months to track titre levels.

Among participants who did not have a previous PCR test but who were deemed to be high risk—ie, had symptoms consistent with SARS-CoV-2 infection and were told by a health-care provider that they had presumed infection, lived with someone with confirmed infection, or were health-care workers themselves—37% had IgG antibodies against SARS-CoV-2. This finding suggests that a majority of participants suspected of having COVID-19 actually were not infected with SARS-CoV-2; however, it might also include a false negative rate of our assay (which has a 92% sensitivity) or insufficient time for the assay to capture IgG antibodies in the group of PCR-positive individuals. More than 99% of them were captured due to the testing algorithm that recalled any of them who were negative or had low titres. This indicates an even higher sensitivity for the ELISA antibody test, further underscoring the likelihood that many in the non-PCR-confirmed group did not have SARS-CoV-2. This highlights the importance of expanded PCR testing to improve diagnosis of this disease even in minimally symptomatic individuals.

The 19% of participants who remained PCR positive despite self-reporting full resolution of symptoms bring to light important considerations regarding the possible duration of viral transmission, and the limited usefulness of PCR testing to ensure clearance. This positive PCR finding could represent shedding of non-viable virus, non-infectious genome fragments or viruses engulmed by immune cells, asymptomatic carriers of SARS-CoV-2, or ongoing infection despite full resolution of symptoms. Detection of viral genome even months after resolution of infection has been shown for viruses such as measles virus.\(^9\) So far, studies have indicated that this is not live virus,\(^9\) and further studies are warranted to determine whether nasopharyngeal PCR positivity is related to transmission and, if so, for how long. This should have substantial implications in terms of guidance of when individuals who have recovered from SARS-CoV-2 infection should end self-isolation; the current CDC recommendation is at least 10 days after symptom onset with at least 72 h without fever off of antipyretics. If PCR positivity is a result of identifying non-infectious genome or non-viable virus, it might be necessary to avoid use of PCR as a definition of clearance of SARS-CoV-2.

There are limitations to our evaluation. Most participants had mild disease, and thus these data might not reflect PCR or antibody findings in a moderately or severely ill population. Participants were recruited based on self-referral in the context of a convalescent plasma donation programme; although individuals were not monetarily reimbursed for their testing, they received antibody results before widespread availability of antibody testing. Additionally, all individuals self-reported their PCR dates and symptom timing, which might have led to recall bias in terms of dates of symptom onset, resolution, and duration, and might have led us to miss asymptomatic carriers who did not inquire about testing. Additionally, given recruitment via an English-language survey and our use of a single collection site, our sample findings might not be generalisable to a more diverse patient population. Given online recruitment, our sample probably also included individuals younger than those most affected with symptomatic COVID-19. Furthermore, we did not collect rigorous data regarding symptom severity, which could potentially be related to the timeline and strength of IgG antibody response to SARS-CoV-2.

Future studies are planned to help us to understand the magnitude and duration of the IgG response in patients who have recovered from SARS-CoV-2 infection, and what antibody titre might be necessary to protect individuals from reinfection. We also hope to better understand which, if any, patients do not mount an IgG immune response. Finally, the clinical significance of prolonged positive SARS-CoV-2 nasopharyngeal PCR in the absence of symptoms requires further clarification.

Duration of nasopharyngeal SARS-CoV-2 PCR detection and time to mount IgG antibody response have important implications for the spread of this virus and risk for reinfection among individuals. In our sample, we found that 19% of people continue to have nasopharyngeal PCR positivity 2 or more weeks after symptom resolution, and that it takes 3 or more weeks to mount an IgG antibody response believed to be potentially protective against future infection. Reassuringly, we found that almost all participants with confirmed SARS-CoV-2 infection in our study mounted an IgG immune response to this disease. Taken together, these findings will be pivotal in understanding disease activity of SARS-CoV-2 moving forward.

**Contributors**

AW, MM, EI, NMB, and GP enrolled patients. AF-B, RM, JJ, MG, JH, IB, ES, and AP-M analysed samples. AW, MM, and EI did the statistical analysis. AW, MM, and FK analysed the data. AW, MM, EL, and FK wrote the manuscript. All authors read and edited the manuscript.

**Declaration of interests**

Mount Sinai has licensed serological assays to commercial entities and has filed for patent protection. Mount Sinai and the Icahn School of Medicine at Mount Sinai, New York, NY, USA) supports work on SARS-CoV-2 immunity in the Krammer laboratory.

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References

1. Chang D, Mo G, Yuan X, et al. Time kinetics of viral clearance and resolution of symptoms in novel coronavirus infection. Am J Respir Crit Care Med 2020; 201: 1150–52.

2. Lan L, Xu D, Ye G, et al. Positive RT-PCR test results in patients recovered from COVID-19. JAMA 2020; 323: 1502.

3. Xiao AT, Tong YX, Zhang S. Profile of RT-PCR for SARS-CoV-2: a preliminary study from 56 COVID-19 patients. Clin Infect Dis 2020; published online April 19. https://doi.org/10.1093/cid/ciaa460.

4. Chu CM, Leung WS, Cheng VC, et al. Duration of RT-PCR positivity in severe acute respiratory syndrome. Eur Respir J 2005; 25: 12–14.

5. Wu F, Wang A, Liu M, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv 2020; published online April 20. https://doi.org/10.1101/2020.03.30.20047365 (preprint).

6. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci USA 2020; 117: 9490–96.

7. Bloch EM, Shoham S, Casadevall A, et al. Deployment of convalescent plasma for the prevention and treatment of COVID-19. J Clin Invest 2020; 130: 2757–65.

8. Sun C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020; 323: 1582.

9. Amanat F, Stadlbauer D, Strohmeier S, et al. A serological assay to detect SARS-CoV-2 seroconversion in humans. Nat Med 2020; 26: 1033–36.

10. Stadlbauer D, Amanat F, Chromikova V, et al. SARS-CoV-2 Seroconversion in humans: a detailed protocol for a serological assay, antigen production, and test setup. Curr Protoc Microbiol 2020; 57: e100.

11. Pujadas E, Ibhe N, Hernandez MM, et al. Comparison of SARS-CoV-2 detection from nasopharyngeal swab samples by the Roche cobas 6800 SARS-CoV-2 test and a laboratory-developed real-time RT-PCR test. J Med Virol 2020; 92: 1695–98.

12. Moran A, Beavis KG, Matushek SM, et al. Detection of SARS-CoV-2 by use of the Cepheid Xpert Xpress SARS-CoV-2 and Roche cobas SARS-CoV-2 assays. J Clin Microbiol 2020; 58: e00772-20.

13. Broder K, Babiker A, Myers C, et al. Test agreement between Roche cobas 6800 and Cepheid GeneXpert Xpress SARS-CoV-2 assays at high cycle threshold ranges. J Clin Microbiol 2020; 58: e01187-20.

14. Craney AR, Velu P, Sallin MJ, et al. Comparison of two high-throughput reverse transcription-polymerase chain reaction systems for the detection of severe acute respiratory syndrome coronavirus 2. J Clin Microbiol 2020; 58: e00890-20.

15. US Food and Drug Administration. Accelerated emergency use authorization (EUA) summary COVID-19 ELISA IgG antibody test (Mount Sinai Laboratory). https://www.fda.gov/media/137029/download (accessed June 1, 2020).

16. Wajnberg A, Amanat F, Firpo A, et al. SARS-CoV-2 infection induces robust, neutralizing antibody responses that are stable for at least three months. medRxiv 2020; published online July 17. https://doi.org/10.1101/2020.07.14.20151126 (preprint).

17. Cao WC, Liu W, Zhang PH, Zhang F, Richardus JH. Disappearance of antibodies to SARS-associated coronavirus after recovery. N Engl J Med 2007; 357: 1962–63.

18. Al-Abdely HM, Midgley CM, Alkhameis AM, et al. Middle East respiratory syndrome coronavirus infection dynamics and antibody responses among clinically diverse patients, Saudi Arabia. Emerg Infect Dis 2019; 25: 753–66.

19. Huang AT, Garcia-Carreras B, Hitchings MDT, et al. A systematic review of antibody mediated immunity to coronaviruses: antibody kinetics, correlates of protection, and association of antibody responses with severity of disease. medRxiv 2020; published online April 17. https://doi.org/10.1101/2020.04.14.20065771 (preprint).

20. US Food and Drug Administration. EUA authorized serology test performance. Aug 17, 2020. https://www.fda.gov/media/137029/download (accessed June 1, 2020).

21. Al-Janabi H, Koyos RD, Adams RJ, Grenfell BT, Griffin DE. Prolonged persistence of measles virus RNA is characteristic of primary infection dynamics. Proc Natl Acad Sci USA 2018; 105: 14989–94.

22. US Centers for Disease Control and Prevention. Duration of isolation and precautions for adults with COVID-19. Sept 10, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html (accessed June 1, 2020).