

PERIOD OF PRESYMPTOMATIC TRANSMISSION

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QUESTION

Transmission of SARS-CoV-2 before onset of symptoms in the index is known, and this is supported by data on viral shedding.

Based on the assumption that the viral load in the upper respiratory tract is highest one day before and the days immediately after onset of symptoms, current procedures for contact tracing (high and low risk contacts), go back two days before start of symptoms in the index (or sampling date in asymptomatic persons) (1), (2), (3). This is in line with the ECDC and WHO guidelines to consider all potential contacts of a case starting 48h before symptom onset (4) (5).

The question was asked whether this period should be extended.

BACKGROUND

Viral load

According to ECDC and WHO, viral RNA can be detected from one to three days before the onset of symptoms (6,7).

The highest viral loads, as measured by RT-PCR, are observed around the day of symptom onset, followed by a gradual decline over time (1,3,8–10)

Period of transmission

A much-cited study by He and colleagues and published in Nature used publicly available data from 77 transmission pairs to model infectiousness, using the reported serial interval (the period between symptom onset in infector-infectee) and combining this with the median incubation period. They conclude that infectiousness peaks around symptom onset. The initial article stated that the infectious period started at 2.3 days before symptom onset. However, a Swiss team spotted an error in their code and the authors issued a correction, stating the infectious period can start from as early as 12.3 days before symptom onset (11). Nevertheless, the new calculations still indicate that <0.1% of the transmissions take place before 7 days prior to symptom onset, 1% of the transmissions more than 5 days and 9% of the transmissions takes place before 3 days prior to the onset of symptoms. The authors therefore recommend to start contact tracing 3 days prior to the onset of symptoms, which would capture 91% of infections (9). They do not mention the proportion of infections that are captured when starting to trace from 2 days before symptom onset, but based on calculations from the Swiss group that spotted the error, we can estimate that changing from 2 to 3 days prior to symptom onset would mean capturing an additional 19% of *presymptomatic* infections or 8% of total infections (12). To bear in mind is that the data from the infector-infectee pairs come from a place/period where symptomatic cases were quickly isolated, so that presymptomatic transmission becomes relatively more important.

That transmission more than 2 days before symptom onset is possible, though rare, is also illustrated by data from cluster investigations. For example, upon examination of 7 clusters in Singapore where presymptomatic transmission occurred, there was one cluster with transmission 3 days prior to symptom onset, for three clusters transmission was 1-2 days before symptom onset and in the remaining three

clusters exposure was continuous and time of infection therefore could not be established (13). In South Korea, a large outbreak occurred among fitness instructors and attendees where the index patient developed symptoms only 3 days after the workshop (14).

Relative importance of presymptomatic transmission

There is still much uncertainty about the impact of presymptomatic transmission on the overall dynamics of the pandemic. It is difficult to determine the proportion of transmission before and after the start of symptoms of an index with case studies, because there is little or no information about the number of (close) contacts of asymptomatic / presymptomatic COVID-19 cases that did not result in an infection. A systematic review found that in modelling studies, 40 to 60% of all SARS-CoV-2 infections are the result of transmission from pre-symptomatic individuals, with a smaller contribution from asymptomatic individuals (15). For instance, in Singapore and China, modelling showed that presymptomatic contamination contributes to 48% and 62% of transmissions in, respectively (16). In the study of Xi He and colleagues, a proportion of 44% presymptomatic transmission is assumed (9). As mentioned above, the presence of strict control measures and rapid isolation of symptomatic patients will influence the relative importance of presymptomatic transmission.

In contrast with the high reported proportions from modelling studies, observed asymptomatic/presymptomatic transmission studied in contact tracing studies is much lower than predicted by COVID-19 transmission models. In Singapore, during the period from 23/01-16/03, only 10/157 (6,4%) locally acquired cases were caused by presymptomatic transmission (13).

Several studies suggest that persons without symptoms are less likely to transmit the virus than those with symptoms. Four individual studies from Brunei, Guangzhou China, Taiwan, and the Republic of Korea have shown that between 0% and 2.2% of people without symptoms at the moment of contact have infected someone else, compared with 0.8% to 15.4% of people with symptoms (17)(18)(19,20). In the study in Brunei, household attack rates of symptomatic cases were higher (14.4% [95%CI: 8.8,19.9]) than presymptomatic cases (6.1% [95%CI: 0.3,11.8]). A study in China looked at the ratio of presymptomatic versus post-symptomatic transmission and examined 468 COVID-19 cases. They reported that 12.6% of transmission occurred prior to the onset of symptoms (21).

Policy in surrounding countries and international guidelines

At the time of the drafting of this document, our neighbouring countries France, Germany and The Netherlands consider the period of 48 hours before start of symptoms, as well as the UK.

ECDC does not indicate a time frame in their definition of close contact. Their latest guidance on contact tracing dates from 9th April and suggests to use a period of 48h before symptom onset (22). Both WHO (interim guidance last updated 10th of May (23)) and the US CDC consider the period from 2 days before symptom onset until the person is isolated.

PRACTICAL ELEMENTS TO CONSIDER

- The greatest risk of infection is in household contacts. In this group, it will make little difference whether the current period of two days is extended by one or several days.
- A better compliance with the general preventive measures (physical distancing, hygienic measures, limiting social contacts) might have more impact than extending the period of contact tracing.
- People might become reluctant to submit to testing if they fear an “irrationally” high number of contacts might be put in quarantine. The number of close contacts that are being reported to the call center remains rather low on average.
- Considering a delay of at least 1-2 days between symptom onset and being contacted by the call center (i.e. having had a test, have the test result available and be reached),
 - it might be hard to remember close contacts from 5 days earlier
 - the implication of tracing these contacts might be limited, since they will only be identified at the earliest on day 5 after exposure
- Changes in contact tracing have repercussions on GP's, scripts, training of the call agents.
- The general public gets more difficult to motivate. Changes in the approach of the pandemic have to be well balanced and need good communication.

RECOMMENDATION

With the current information derived from a limited amount of studies, it is recommended to keep the period for contact tracing at 2 days before start of symptoms in the index (or sampling date in asymptomatic persons).

The same period should be used both in contact tracing by call agents and by the app.

If more information becomes available, this period might be re-evaluated and extended if necessary.

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