

## SYNOPSIS

# (ARCHIVED) COVID-19 – What We Know So Far About... The Period of Communicability

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## ARCHIVED DOCUMENT

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## Introduction

“What We Know So Far” documents are intended to provide an overview of some of the published and unpublished reports related to emerging issues with respect to coronavirus disease 2019 (COVID-19). The reports are found through ongoing scanning of the published literature and other reports, as appropriate. It is recognized that there may be additional information not captured in this document. As this is a rapidly evolving outbreak, the information will only be current as of the date the document was written.

## Key Points

This document summarizes the evidence for the period of communicability of SARS-CoV-2, the virus responsible for COVID-19. For clarity, in this document we will use the term COVID-19 to refer to both the virus and the disease.

- The definitive period of communicability for COVID-19 is **not known at this time**.
- **Earliest time of communicability:** There are studies reporting that COVID-19 can be transmitted from people who are in their incubation period. **Some studies have suggested transmission as early as five days before symptom onset.** These studies are case reports and much of this evidence is from China. Due to circulation of COVID-19 in China at the time of these case reports, it is possible that there was another unrecognized source of infection, instead of the individuals who are described as the source case in these studies.
- **Latest time of communicability:** There is evidence of the presence of COVID-19 RNA in patient samples for as long as **several weeks** after symptom onset. However, RNA detection by itself does not necessarily indicate the presence of live virus.

- One study found that virus can be grown from some upper respiratory samples collected during **the first eight days after symptom onset** with negative samples afterwards to day 13. However, this study has not yet been peer-reviewed and included only nine patients who all had mild symptoms.
- Another study found that COVID-19 virus could be isolated from a stool sample, which was collected 15 days post symptom onset.

## Background

The period of communicability is the time period during which an infected person can spread their infection to others. It is expressed as a range from the earliest time to the latest time infected people can be communicable to others. The communicable period is important to determine the time frame for assessing who is a contact based on their exposure to the case, and for determining when a case no longer requires isolation.

## Earliest Time of Communicability

The earliest time individuals can be communicable would be during their incubation period (the period from exposure to onset of symptoms). Several studies, summarized below, support transmission of COVID-19 during the incubation period.

## Evidence of COVID-19 RNA in Respiratory Samples Collected in the Incubation Period

- A study by [Pan et al.](#) found COVID-19 RNA in a throat swab and a sputum sample from two different individuals taken one day before their onset of symptoms; both individuals were being swabbed because of a history of exposure to a known case. However, RNA detection alone does not necessarily indicate the presence of live virus.

## Evidence of COVID-19 Transmission in the Incubation Period

Several studies describe potential transmission in the incubation period or in the early symptomatic period. In most instances, the family members or colleagues who acquired the infection reported no other known sources of exposure other than a case who was in their incubation or early symptomatic period.

- [Rothe C et al.](#) was the first study published that described potential transmission during the incubation period. This was a case report of an individual from China who attended three days of meetings in Germany with business partners and was initially thought to be asymptomatic until the day she flew home. She then tested positive for COVID-19 upon returning to China, following which it was discovered that some of her German colleagues were infected, too. Upon further investigation, additional information from the source case indicated that she had experienced some mild non-specific symptoms while in Germany.

Although the first German case was infected by the individual from China (source case), another two German cases did not have exposure to the source case and may have been infected by the first German case. Of these two cases, one had their last exposure to the first German case one

day after the first case's exposure to the individual from China and three days before the first German case's onset of symptoms.

**Therefore, this study suggests that transmission may have occurred one day after exposure and three days before symptom onset. It also demonstrates transmission with very early and non-specific symptoms.**

- Several other studies describing infections in China suggest transmission during the incubation period. It should be noted that, due to circulation of COVID-19 in China during this time, it is possible that there was another unrecognized source of infection, in addition to the cases reported in these studies.
  - [Yu P et al.](#) described an 88-year-old man from Shanghai who developed symptoms five days after the arrival of two visitors from Wuhan. The two visitors developed symptoms after the man with the earliest symptom onset among the two visitors occurring 11 hours after the man's first symptoms. This suggests that at least one of the visitors had spread infection in their incubation period. Assuming the visitor with the earliest symptom onset transmitted infection to the man, **the earliest the infection could have occurred is from five days before onset of illness in that visitor**, based on the date of the visitors' arrival. The latest the infection could have occurred is dependent on the incubation period in the man. Assuming a very short incubation period of only one day, **the visitor would have been infectious just over one day before symptom onset.**
  - [Huang R et al.](#) described a patient from near Wuhan who visited her family in Nanjing and did not develop symptoms until four days after leaving Nanjing. She infected six family members, some of whom she lived with and some with whom she attended one or more family dinners with, including one on the day before her departure from Nanjing. Two family members, who appear to have been infected at the family dinner with the visiting woman the day before her departure, attended another family dinner with three different relatives. This occurred on the day after the dinner with the visiting woman, and three and four days before the onset of symptoms. The three relatives subsequently developed symptoms and were found to be infected with COVID-19.

**This study suggests that transmission can occur at least five days before symptom onset and also suggests that transmission may occur as early as one day following exposure.**

- [Tong ZD et al.](#) reported a case of COVID-19 from Wuhan who attended a conference in Zhoushan, China three days before illness onset. Two colleagues from Zhoushan also attended the conference and dined with the case the following day (two days before illness onset), sharing the same serving plates. The two colleagues were subsequently confirmed to be infected. **This suggests that the source patient likely infected his two colleagues at least two days prior to symptom onset.**

## Studies Comparing the Incubation Period and the Serial Interval

The serial interval is the time from onset of symptoms in one case to the time of symptom onset in the case(s) they infect. When the serial interval is shorter than the incubation period, some transmission is likely to have occurred in the incubation period. Some studies (for example, [Nishiura H et al](#) and [Du Z et](#)

al.) found a short serial interval ranging from a mean of 3.96 days to a median of 4.6 days. This is shorter than the mean incubation period of five days referenced by Nishiura et al., suggesting transmission during the incubation period.

## Latest Time of Communicability

### Studies that Assess the Presence of Viral RNA

The presence of RNA in specimens from infected individuals can provide information about the potential for communicability. Some studies report the presence or absence of COVID-19 RNA as detected by real-time reverse transcriptase polymerase chain reaction (RT-PCR), while others also estimate viral loads in the samples. It should be noted that RNA detection by RT-PCR does not necessarily indicate the presence of live virus.

A number of studies assessing viral RNA by RT-PCR are summarized in Table 1. Most determined the presence of viral RNA relative to the onset of symptoms. **Although viral load appeared to decrease over time, a number of studies showed prolonged detection of RNA, some up to three weeks or longer from symptom onset.** Notably, the levels of viral RNA detected during prolonged periods were low and are likely to represent remnants of viral RNA and not live virus, although there are insufficient viral culture studies at this time to confirm this.

**Table 1: Summary of Studies that Assess Viral Load by RT-PCR using Serial Samples from Patients with COVID-19**

Study	Key Features	Swab Type and RT-PCR Results
<a href="#">Bai Y et al.</a>	Asymptomatic individual; RT-PCR testing based on last exposure to Wuhan	Nasopharyngeal swabs: <ul style="list-style-type: none"> <li>Positive on day 18 after leaving Wuhan; negative on days 16, 26 and 29</li> </ul>
<a href="#">Cai J et al.</a>	Case series of 10 children	Nasopharyngeal and throat swabs: <ul style="list-style-type: none"> <li>Positive for 6 to 22 days from symptom onset (mean 12 days) and undetectable thereafter</li> </ul> Stool: <ul style="list-style-type: none"> <li>Positive for at least 18 to 30 days from symptom onset in 5 of 5 children with positive stools</li> </ul>
<a href="#">Holshue M et al.</a>	First confirmed COVID-19 case in the US	Nasopharyngeal swabs: <ul style="list-style-type: none"> <li>Positive on days 4, 7, 11, and 12 of illness with decreasing viral load; no additional tests performed</li> </ul> Oropharyngeal swabs: <ul style="list-style-type: none"> <li>Positive on days 4, 7, 11 of illness with decreasing viral load; negative on day 12</li> </ul> Stool:

Study	Key Features	Swab Type and RT-PCR Results
		<ul style="list-style-type: none"> <li>Positive on day 7 of illness with low viral load; only tested on that day</li> </ul>
<a href="#">Lan L et al.</a>	<p>Follow up of 4 recovered patients meeting criteria for hospital discharge or discontinuing isolation (including symptom resolution and two consecutive negative RT-PCR results on throat swabs). Time to recovery ranged from 12 to 32 days</p>	<p>After meeting release criteria with two negative RT-PCR results on throat swabs and then waiting an additional 5 days, repeat throat swabs were done 5 to 13 days later and were positive, as were an additional 3 swabs over the next 4-5 days</p>
<a href="#">Hu Z et al.</a>	<p>24 initially asymptomatic individuals identified through contact tracing, five of whom subsequently developed symptoms</p>	<p>Pharyngeal swabs:</p> <ul style="list-style-type: none"> <li>Interval from first day of RT-PCR positive to first day of continuous negative ranged from 1 to 21 days (median 9.5 days)</li> </ul>
<a href="#">Kam K et al.</a>	<p>Generally well baby hospitalized due to lack of a caregiver and monitored daily for at least 18 days</p>	<p>Nasopharyngeal swabs:</p> <ul style="list-style-type: none"> <li>Daily swabs were positive until day 16 after admission, with viral loads decreasing over time, and negative on day 17</li> </ul> <p>Urine samples:</p> <ul style="list-style-type: none"> <li>Negative on day two of admission</li> </ul> <p>Stool:</p> <ul style="list-style-type: none"> <li>Negative on day two of admission but tested positive on day nine at relatively low levels</li> </ul>
<a href="#">Pan Y et al.</a>	<p>Serial respiratory samples from two patients Respiratory samples from 80 individuals collected at various stages of infection</p>	<p>Serial respiratory samples (two patients; throat swab and sputum samples):</p> <ul style="list-style-type: none"> <li>Viral load peaked 5-6 days after symptom onset</li> <li>Positive until day 8 (throat swab) and day 6-11 (sputum) followed by subsequent negatives</li> </ul> <p>Respiratory samples (80 individuals; nasal [n=1], throat swabs [n=67], and sputum [n=42]):</p> <ul style="list-style-type: none"> <li>Detectable up to 15 days post onset in a throat swab from one patient, with no further tests conducted</li> <li>Two individuals (case contacts) tested positive one day prior to symptom onset at high levels</li> </ul> <p>Stool:</p> <ul style="list-style-type: none"> <li>Positive in 9 of 17 cases within 0 to 13 days of onset</li> </ul>

Study	Key Features	Swab Type and RT-PCR Results
<a href="#">Wöelfel R et al.</a> (Not peer-reviewed)	Nine patients with mild symptoms which mostly waned by the end of the first week	Upper respiratory specimens: <ul style="list-style-type: none"> <li>• Viral load peaked before day 5 and declined over time from symptom onset</li> <li>• Declined more slowly in sputum compared to upper respiratory swab specimens</li> </ul> Multiple sites: <ul style="list-style-type: none"> <li>• In a small number of cases, detected up to 20 days from symptom onset in upper respiratory swabs, 21 days in stool and 22 days in sputum</li> </ul>
<a href="#">Young BE et al.</a>	Multiple specimens on 18 patients over two week period from four hospitals	Nasopharyngeal swabs: <ul style="list-style-type: none"> <li>• Median duration from first PCR positive to last positive was 12 days (range 1-24 days)</li> <li>• Five patients had detectable viral load up to day 20-23 of illness, albeit at low levels</li> </ul> Stool: <ul style="list-style-type: none"> <li>• PCR positive in 4/8 (50%) patients between day 5-9 of illness</li> </ul>
<a href="#">Zhou F et al.</a>	Retrospective cohort study of adult inpatients from two hospitals (191 patients – 137 discharged, 54 died)	Respiratory specimens: <ul style="list-style-type: none"> <li>• Among survivors, median duration of positivity for throat swabs was 20 days (range 8-37 days) after symptom onset (no quantitative results provided)</li> <li>• Among cases that died, RNA was detected until death (death was a median of 18.5 days after symptom onset)</li> </ul>
<a href="#">Zhou P et al.</a>	Seven patients in the intensive care unit; five had repeat sampling	Respiratory specimens (bronchoalveolar lavage fluid and/or oral swab): <ul style="list-style-type: none"> <li>• All patients positive 7 to 18 days after symptom onset</li> </ul> Oral swab, anal swab and blood: <ul style="list-style-type: none"> <li>• Negative by 18 to 29 days from symptom onset (five patients, were still symptomatic and hospitalized)</li> </ul>
<a href="#">Zou L et al.</a>	Serial respiratory samples from 18 patients (17 symptomatic; 1 asymptomatic)	Nasal and throat specimens: <ul style="list-style-type: none"> <li>• Higher viral loads detected soon after symptom onset (peaking around day 3-6), and declining in subsequent days</li> <li>• Viral RNA detected at 21 days at low levels in nasal swab from one patient</li> </ul>

## Viral Culture Studies

Communicability is best assessed through detection of live virus using viral culture. Two studies were found that describe viral culture of specimens positive for COVID-19, neither of which are peer-reviewed.

- An article by [Wöelfel et al.](#) describes virologic analyses of nine patients with mild symptoms. Multiple upper respiratory (oro- or nasopharyngeal) swabs, sputum, stool, blood and urine samples were collected after symptom onset.
  - **Viral culture:** Live virus was isolated during the first week of symptoms from 16.7% of upper respiratory swabs and 83.3% of sputum samples; however, no positive cultures were obtained from samples taken after day 8 of symptoms, despite ongoing presence of viral RNA. Live virus was not isolated from stool specimens obtained from four patients tested from days 6 to 12 post symptom onset, despite high viral RNA concentrations.
  - **RT-PCR:** Levels of viral RNA by RT-PCR correlated with virus isolation by culture, where virus was not successfully isolated from respiratory specimens with lower viral loads. Additional details are in Table 1.
- [Zhang Y et al.](#) reported the isolation of COVID-19 virus from one stool sample from a patient with severe pneumonia at 15 days post symptom onset.

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