

SYNOPSIS

04/28/2020

COVID-19 — What We Know So Far About... Routes of Transmission

Introduction

PHO is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). "What We Know So Far" documents are intended to provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

The development of these documents includes a systematic search of the published literature as well as scientific grey literature (e.g., ProMed, CIDRAP, Johns Hopkins Situation Reports) and media reports, where appropriate. Relevant results are reviewed and data extracted for synthesis. All "What We Know So Far" documents are reviewed by PHO subject-matter experts before posting.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in these documents is only current as of the date of posting.

Key Points

- COVID-19 is transmitted via droplets during close, unprotected contact.
- Airborne spread has not been documented for COVID-19, but aerosols may be generated during aerosol generating medical procedures which could theoretically lead to transmission through this route.
- There is no specific evidence documenting transmission through fomites. However, the virus has been detected on surfaces in the patient environment and this is a likely source of transmission based on experience with other coronaviruses.
- While the virus has been detected in the stool and the blood, the roles of fecal-oral and bloodborne transmission remain uncertain.
- There is no conclusive evidence of vertical transmission to date, but further studies are needed.

Background

The purpose of this document is to outline what is known about how COVID-19 is transmitted from person-to-person, based on a review of the scientific literature. The virus responsible for COVID-19 is genetically similar to other coronaviruses. In particular, it shares a high degree of genetic similarity (79% identity) (Lu R et al.), with the coronavirus (CoV) responsible for Severe Acute Respiratory Syndrome (SARS). Therefore, in instances of limited evidence for COVID-19, it is reasonable to extrapolate existing data from other coronaviruses, in particular SARS-CoV.

Droplet and Contact Transmission

Current evidence suggests that the mode of transmission of COVID-19 is through direct contact and respiratory droplets that have the potential to be propelled for varying distances (<u>European Centre for Disease Prevention and Control (ECDCa)</u>, <u>Imai et al.</u>, Schneider et al.).

- The majority of cases have been linked to person-to-person transmission through close direct contact to someone with respiratory symptoms (<u>Burke et al.</u>, <u>Chan et al.</u>, <u>ECDCa</u>, <u>Pung et al.</u>) or close contact with a case in the incubation period who was later confirmed to have COVID-19 (<u>Huang R et al.</u>, <u>Tong et al.</u>, <u>Yu P et al.</u>). High viral loads have been identified in individuals who were asymptomatic or pre-symptomatic (<u>Arons et al.</u>); however, uncertainties remain regarding the role of asymptomatic transmission in driving outbreaks in the absence of major droplet-releasing symptoms (e.g. coughing, sneezing).
- A recent report by the World Health Organization (WHO) Joint Mission on Coronavirus Disease 2019 (COVID-19) in China, summarizes the experience with 75,465 cases and indicates that the route of transmission is droplet during close unprotected contact (WHO)
- Respiratory droplets have been shown to be propelled up to 2 meters (m) in most studies (ECDCa, Imai et al., Schneider et al.) studies and occasionally have been found on the floor up to 13 feet (ft) (or 4 m) away from the patient (Guo et al.).

Conjunctiva

Transmission through the ocular surface is considered a possible route of transmission for COVID-19 based on a recent case report and evidence of virus detection from the eye among cases with conjunctivitis.

- In a case report, the authors describe a healthcare worker who became infected with COVID-19 after visiting a patient wearing an N95 respirator, but no eye protection. The healthcare worker developed eye redness and then pneumonia (<u>Lu C et al.</u>).
- In one study of 30 confirmed COVID-19 cases with pneumonia, tear and conjunctival secretions were collected twice from each patient and tested using reverse transcription polymerase chain reaction (RT-PCR) assays. Only one patient had conjunctivitis with one of two samples yielding a positive RT-PCR result. The remaining 58 samples from all other patients were negative (Xia et al.).
- In a cross-sectional study of 72 laboratory-confirmed cases of COVID-19, two patients (2.8%) had conjunctivitis. Viral RNA fragments were identified in ocular discharges using a RT-PCR assay in one patient with conjunctivitis (Sun et al.).
- In another cross-sectional study, conjunctival RT-PCR assays were conducted on 14 confirmed cases and 16 suspect cases of COVID-19. All results were negative (Xu L et al.).

Airborne Transmission

There is currently no evidence that COVID-19 is transmitted through the airborne route. As more epidemiological data emerge on cases globally, information is becoming available that suggest that airborne transmission is not occurring:

 A recent report from the WHO China Joint Mission on COVID-19 summarizing 75,465 cases indicates that airborne spread has not been reported (WHO). This report states that the majority

- of COVID-19 transmission in China is occurring within families. Of all of the infection clusters investigated, 78-85% were within families, with a household secondary attack rate of 3-10%. The absence of significant clusters in other settings suggests that the mode of COVID-19 transmission is not airborne.
- An article describing the active follow-up of individuals exposed to first ten cases of COVID-19 in the United States describes secondary transmission only to close household contacts. In this article, 445 persons who had contact with one of the cases were identified. Of these, 19 (4%) were household members, 104 (23%) were community members who spent at least 10 minutes in close proximity to the case, 100 (22%) were community members exposed in a healthcare setting and 222 (50%) were healthcare workers. Two persons who were household members of cases of COVID-19 tested positive, for a symptomatic secondary attack rate of 0.45% (2/445) among all contacts and a symptomatic secondary attack rate for all household contacts of 10.5% (2/19) (Burke et al.). The absence of transmission to contacts outside the household setting suggests that the mode of COVID-19 transmission is not airborne. Of note, five household members who were continuously exposed to a case did not become infected.
- Healthcare workers caring for COVID-19 patients in other jurisdictions, including British Columbia, have not acquired COVID-19 while using Droplet and Contact Precautions recommended in the province (Weeks).
- The lack of transmission to passengers seated nearby cases who have travelled on airplanes, does not support an airborne transmission route of COVID-19 (Schwartz et al.).
- Studies have inconsistently detected virus in air sampling:
 - In two studies conducting air sampling around confirmed cases, COVID-19 was not detected (Cheng et al., Ong et al.).
 - One study detected SARS-CoV-2 by PCR in 35% (14/40) air samples in the ICU and 12.5% (2/16) air samples on the general ward where patients with COVID-19 are managed. The majority of these air samples were within 2 m of the patients, with 1/8 samples positive at 4 m away (Guo et al.).
- An investigation of a COVID-19 outbreak in a restaurant in Guangzhou, China determined that
 the air conditioning ventilation likely contributed to droplet transmission. Infections were
 documented in three families after sitting in close proximity (< 1 m) for more than 1 hour. None
 of the other staff or diners were infected, suggesting airborne transmission was unlikely (<u>Lu J et al.</u>).

Airborne Transmission during AGMPs

While airborne transmission has not been documented under routine circumstances (i.e. in community settings and in routine patient care) it may be possible for it to occur when an aerosol-generating medical procedure (AGMP) is performed.

- This is supported by the recent report from WHO, which states that airborne transmission could theoretically occur during an aerosol-generating medical procedure, although there were no documented occurrences in the report (WHO).
- Studies have documented the aerosol stability of SARS-CoV-2
 - In the study by <u>van Doremalen et al.</u>, aerosols were created experimentally (three-jet nebulizer and Goldberg drum) and found to survive up to three hours on surfaces, supporting that aerosols may be generated under certain circumstances (i.e. AGMPs).
- Case series of exposures to COVID-19 patients during AGMPs have not demonstrated transmission to HCWs using droplet/contact precautions (Ng et al., Wong et al.).

- During the SARS outbreak in 2003, infections disproportionately occurred among healthcare workers, with those involved in aerosol-generating procedures and manipulation of the airway (i.e. at the time of intubation) at greatest risk (Booth CM et al.). An investigation into a nosocomial outbreak of SARS in Toronto concluded that the epidemiological links described in their investigation support the theory that SARS is transmitted primarily through respiratory droplets and direct contact, but noted that transmission occurred during high risk procedures (i.e. intubation) when only a surgical mask was utilized, in the absence of protective eyewear (Varia et al.).
- More information on what is currently known about COVID-19 and the risks to healthcare workers can be found in the WWKSF document on the Risks to Health Care Workers.

Fomite Transmission

There is currently no data on the ability of COVID-19 to survive or be transmitted through surfaces. However, there is indirect evidence to support that this is a possible source of transmission:

- Studies have documented the presence of virus on surfaces in the environment of patients who have tested positive for COVID-19 (Ong et al., van Doremalen et al.).
- Other coronaviruses have been observed to remain viable for days to weeks on environmental surfaces. Survival is enhanced at low temperatures (i.e., 4°C vs. 20°C) (ECDCb, Kampf et al.).
- The relative importance of indirect contact transmission (i.e. droplets spreading from a patient to an environmental surface to another individual) for the coronaviruses responsible for SARS and Middle East Respiratory Syndrome (MERS) is also uncertain (Otter et al.).
- Two field studies have evaluated SARS-CoV surface contamination:
 - In a study involving hospitals in Bangkok, Thailand, Taipei, and Taiwan, 24/63 (38%) of surfaces (patient rooms, nursing stations, emergency department, and public spaces) had viral RNA detected by PCR. However all were culture negative (i.e. viable virus could not be grown from the samples) raising uncertainty of the viability of the detected virus and its ability to cause human infection (Dowell et al.).
 - During the 2003 SARS outbreak in Toronto, 85 swabs were taken from 19 patient rooms in Toronto hospitals. A total of 3 (3.5%) were positive (bed table, TV remote, fridge handle in nursing station), however none were culture positive, raising similar questions about the risk for human infection (Booth TF et al.).

Fecal-oral Transmission

While the virus has been detected in the stool, the roles of fecal-oral transmission remains uncertain.

- As part of early investigations of the outbreak, the virus responsible for COVID-19 has been
 detected and isolated in the intestinal tissues of animals challenged with the virus (<u>WHO</u>).
- Tissues in the oral cavity express angiotensin-converting enzyme 2 (ACE2) receptors that are believed to be used by COVID-19 to enter cells (Xu H et al.). ACE2 receptors have also been documented in the cytoplasm of gastrointestinal epithelial cells (Xiao et al.).
- It has been reported that a small proportion of patients experience diarrhea and vomiting during COVID-19 infection (<u>Chen N et al.</u>, <u>Guan et al.</u>, <u>Wang D et al.</u>), with case reports of gastrointestinal symptoms in the absence of respiratory symptoms (<u>Hosoda et al.</u>, <u>Song et al.</u>).
- COVID-19 RNA has been detected in stool in various studies, with prolonged shedding for up to
 4-5 weeks in moderate cases and pediatric cases (<u>Chen L et al.</u>, <u>Tang et al.</u>, <u>Wu et al.</u>).

Live virus has reportedly been cultured from stool, in some cases (<u>Wang W et al.</u>, <u>WHO</u>, <u>Pan et al.</u>, <u>Zhang et al.</u>).

- A case report found SARS-CoV-2 RNA detection and intracellular staining of viral nucleocapsid
 protein in gastric, duodenal, and rectal epithelia demonstrating that SARS-CoV-2 infects these
 gastrointestinal glandular epithelial cells (Xiao et al.).
- The WHO-China Joint Mission Document notes that viral RNA has been detected in feces in up to 30% of patients from day 5 following onset of symptoms and in some cases has been detected for up to 4-5 weeks (WHO).
- More information on fecal-oral transmission can be found in the What We Know So Far (WWKSF) document on fecal-oral transmission.

Bloodborne Transmission

While the virus has been detected in the blood, the role of bloodborne transmission remains uncertain.

- Several studies have reported detection of COVID-19 RNA, in either plasma or serum (<u>Chan et al.</u>, <u>Huang C et al.</u>, <u>Wang W et al.</u>).
- More information on bloodborne transmission can be found in the <u>WWKSF document on bloodborne transmission</u>.

Vertical Transmission

To date, there has been no conclusive evidence of vertical transmission of COVID-19 from mother to child. Although several case reports suggest that it may be possible, the reported case series to date suggest that it is not a common occurrence.

- The following studies have shown no evidence of vertical transmission:
 - <u>Khan et al.</u> reported no vertical transmission after three pregnant women with COVID-19 delivered naturally; children had normal birth weights, lengths, and Apgar scores.
 - Zhu et al. reported no vertical transmission after 9 pregnant women with COVID-19 delivered; findings were confirmed with throat swabs taken at one to nine days after birth and there was no evidence of vertical transmission.
 - <u>Fan et al.</u> reported no vertical transmission after two pregnant women with COVID-19 delivered and both infants were in good health.
 - <u>Chen R et al.</u> reported no vertical transmission after 17 pregnant women with COVID-19 delivered via Caesarean section. Three births were premature, but newborns were over 2500 g and children were discharged in good health following brief observation in the NICU. Lack of infection was confirmed with nasal swabs performed one day after birth and again on the day before discharge.
 - <u>Chen H et al.</u> reported no vertical transmission after 9 pregnant women with COVID-19 pneumonia delivered via Caesarean section. SARS-CoV-2 could not be detected in amniotic fluid, cord blood, breast milk, or from neonatal throat swabs.
 - <u>Liu et al.</u> reported no vertical transmission after 10 pregnant women with COVID-19 delivered via Caesarean section. There was no clinical or serologic evidence suggestive of vertical transmission.

- Yu N et al. reported unlikely vertical transmission after 3 pregnant women with COVID-19 delivered via Caesarean section. One of the newborns contracted the virus **36 hours** after birth. SARS-CoV-2 was not detected in the placenta or cord blood in this patient.
- Yang et al. reported no vertical transmission after a pregnant woman with COVID-19
 delivered via Caesarean section. An oropharyngeal swab, obtained immediately after birth,
 indicated the newborn was negative. During the next 2 days, the infant's oropharyngeal
 swab, blood, feces, and urine samples remained negative for SARS-CoV-2 throughout
 testing at 7 different time points.
- The following studies provide some evidence that vertical transmission of COVID-19 may occur, but do not provide conclusive evidence. The interpretation of antibody testing for SARs-CoV-2 is an evolving area and concerns around possible cross-reactivity and specificity need to be considered.
 - Zeng L et al. reported possible vertical transmission in 3 of 33 neonates who were born to
 mothers with confirmed COVID-19 pneumonia. They report that because 'strict infection
 control and prevention procedures were implemented during the delivery' it is likely that
 the source of infection was maternal, but details of these practices are not provided.
 Neonates were diagnosed based on swab results done on Day 2 of life.
 - Zeng H et al. reported possible vertical transmission in 2 of 6 neonates who were born to
 mothers with COVID-19 pneumonia at Zhongnan Hospital of Wuhan University and
 delivered via Caesarean section. All mothers wore masks, and all medical staff wore
 protective suits and double masks. The infants were isolated from their mothers
 immediately after delivery. Neonatal throat swabs and blood samples collected at birth all
 had negative RT-PCR test results. All 6 infants had antibodies detected in their serum, 2
 infants had IgG and IgM concentrations higher than the normal level (<10 AU/mL).
 - Dong et al. reported potential vertical transmission in a newborn who was born to a
 mother at 34 weeks gestation with COVID-19 and delivered via Caesarean section. The
 mother wore an N95 mask and did not hold the infant. The neonate had no symptoms and
 was immediately quarantined in the neonatal intensive care unit. At 2 hours of age, the
 COVID-19 IgG level was 140.32 AU/mL and the IgM level was 45.83 AU/mL.
 Nasopharyngeal swabs taken from 2 hours to 16 days of age were negative.
 - <u>Alzamora et al.</u> reported possible vertical transmission in a newborn born by Caesarean section to a mother with COVID-19 pneumonia (4 days of symptoms). The infant was isolated immediately after birth without delayed cord clamping or skin-to-skin contact. Nasopharyngeal swab at 16 hours of life was positive for COVID-19. The serology testing for IgM and IgG were negative.

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Citation

Ontario Agency for Health Protection and Promotion (Public health Ontario). COVID-19 – What we know so far about... routes of transmission. Toronto, ON: Queens's Printer for Ontario; 2020

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