SYNTHESIS

12/01/2020

COVID-19 Routes of Transmission – What We Know So Far

Introduction

Public Health Ontario (PHO) is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents 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.

See Appendix A for Glossary of Terms for COVID-19 Routes of Transmission.

Updates in Latest Version

Since the last version (July 16, 2020), multiple new studies and systematic reviews have been published with evidence on the potential for transmission via several routes including respiratory droplet and close-contact, vertical, conjunctival and fomite transmission. There was more evidence against several modes of transmission, including sexual and transmission through breast milk.

Importantly, there are now experimental studies and outbreak case studies that support severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission through small particle respiratory droplets or aerosols during prolonged exposure in a poorly ventilated space. The primary mode of SARS-CoV-2 transmission; however, remains through respiratory droplets and unprotected close contact.

New modes of transmission addressed in this update include potential transmission from wastewater, food, urine and zoonotic transmission (through animals).

Key Points

- Overall, the evidence for various transmission routes relies heavily on the detection of viral RNA in clinical and environmental samples, rather than the detection of viable, infectious virus. Further, the quantity of viral RNA that is representative of an infectious dose is unclear.
• Transmission of SARS-CoV-2 occurs predominantly through close (<2 m), unprotected contact with an infected individual(s). Based on the epidemiology of COVID-19, transmission predominantly occurs via respiratory droplets from symptomatic, presymptomatic or less commonly, asymptomatic individuals.

• Transmission over longer distances (>2 m) is less common, but possible under certain conditions such as prolonged exposure in a poorly ventilated space. Under these conditions, inhalation of small particle respiratory droplets and aerosols can occur. SARS-CoV-2 is likely an opportunistic airborne pathogen, as non-airborne transmission is most common, but aerosols may result in transmission under favourable conditions.

• Relatively uncommon routes of transmission of SARS-CoV-2 include conjunctival, vertical (intrauterine), fecal-oral, fomite and zoonotic. While these routes of transmission are possible, their contribution to the epidemiology of COVID-19 is unclear.

• Routes of transmission that are theoretically possible due to the detection of viral RNA, but that are very unlikely, are sexual transmission (via semen and vaginal secretions); bloodborne transmission (blood products, organ transplant); transmission through breast milk; transmission through urine; food-borne transmission; and transmission through contaminated wastewater.

Background

The purpose of this document is to outline the evidence for various SARS-CoV-2 transmission routes, based on a review of the scientific literature. SARS-CoV-2 is genetically similar to other coronaviruses and shares a high degree of genetic similarity (79%) with the coronavirus (SARS-CoV-1) responsible for Severe Acute Respiratory Syndrome (SARS). Therefore, in instances of limited evidence for COVID-19, we have extrapolated existing data from other coronaviruses, in particular SARS-CoV-1.

During the COVID-19 pandemic, evidence for and against potential routes of transmission has evolved. In some instances, there is no consensus on the contribution from certain modes of transmission. A number of reports postulate transmission routes; however, in many it is challenging to determine the precise mode of transmission where there are multiple opportunities for transmission to occur (i.e. through direct contact, fomites, or inhalation). In addition, the strength of evidence by transmission route has changed. In contrast to the July 16, 2020 version of this document, there have been several systematic reviews published on the subject that are included. The systematic reviews contribute to bringing the evidence base closer to a consensus. Within this document, we underpin our findings with systematic reviews and meta-analyses where available, supporting findings with case series and cohort studies.

Methods

In considering feasibility, scope and the need for responsiveness, a rapid review was chosen as an appropriate approach to determining the routes of transmission for SARS-CoV-2. A rapid review is a type of knowledge synthesis wherein certain steps of the systematic review process are compromised in order to be timely.

PHO is actively monitoring, reviewing and assessing relevant information related to COVID-19. This document provides a rapid review of the evidence related to transmission routes of SARS-CoV-2.

On October 14, 2020, PHO Library Services developed and conducted a search in MEDLINE (Appendix B). English language peer-reviewed and grey literature records that describe transmission of SARS-CoV-2
were included. We did not restrict year of publication. We reviewed references of included studies for additional articles.

Two reviewers screened titles and abstracts, and the senior author reviewed the application of the eligibility criteria. The senior author synthesized relevant data. We did not perform a critical appraisal of the methodological quality of studies due to time constraints. PHO subject matter experts reviewed this rapid review before posting.

Results

Droplet and Contact Transmission

Current evidence suggests that the primary mode of transmission of COVID-19 is through direct contact from respiratory droplets that have the potential to be propelled for varying distances.\(^3\,^5\)

**Household secondary attack rates are indicative of predominantly droplet and close-contact transmission:**

In household settings, people are in close proximity to one another, thereby increasing the risk of infection. The consensus among systematic reviews is that most infections are occurring in household settings where physical distancing is not feasible and household secondary attack rates are higher than in casual-contact settings (e.g., shopping).

In a systematic review and meta-analysis, Lei et al. reported the secondary attack rate in households was 27% (95% confidence interval [CI]: 21–32); the risk of secondary infection was 10 times higher in households compared to non-household settings (odds ration [OR]: 10.72; 95% CI: 5.70–20.17; \(p<0.001\)).\(^7\) In another systematic review and meta-analysis by Madewell et al., the household secondary attack rate was 18.8% (95% CI: 15.4–22.2).\(^8\) Koh et al, in a meta-analysis, reported that the household secondary attack rate was 18.1% (95% CI: 15.7–20.6), much higher than the secondary attack rate in health care settings (0.7%; 95% CI: 0.4–1.0).\(^9\) Further, these findings do not support predominant airborne transmission. If SARS-CoV-2 was predominantly and efficiently spread through an airborne route (i.e., through aerosols), household secondary attack rates would be expected to be substantially higher (e.g., >90% in measles).\(^6\)

Contact tracing studies also show higher secondary attack rates in households, compared to other settings. The limited transmission to contacts outside the household setting suggests that the mode of SARS-CoV-2 transmission is predominantly from close contact. Luo et al. studied 3,410 close contacts of 391 index cases in Guangzhou, China and found that the secondary attack rate was lower when people were exposed in health care settings (1.0%; OR: 0.09; 95% CI: 0.04–0.20) and on public transportation (0.1%; OR: 0.01; 95% CI: 0.00–0.08), compared to the household secondary attack rate (10.3%).\(^10\) In a retrospective cohort study in Guangzhou, China, Jing et al. reported the household secondary attack rate (among close relatives) was 12.4% (95% CI: 9.8–15.4).\(^11\) In most studies, non-household close contacts have secondary attack rates less than 1% (Bi et al., Chaw et al., Cheng et al., Li et al.).\(^12\,^15\)

**Evidence for SARS-CoV-2 droplet and contact transmission:**

The majority of COVID-19 cases have been linked to person-to-person transmission through close, direct contact with symptomatic patients,\(^16\,^18\) or through close contact with a pre-symptomatic patient.\(^19\,^21\) In addition, high viral loads have been identified in individuals who were asymptomatic or pre-
symptomatic. In a case-control study of patients 18 years old and older in the United States (US), Fisher et al. reported that close contact with a person with COVID-19 was reported more often among cases (42%) than controls (14%). A study modelling the transmission risk from epidemiological data among train passengers revealed that travellers directly adjacent to the index patient had a much higher infection risk (relative risk [RR]: 18.0; 95% CI: 13.9–23.4), and the attack rate decreased with increasing distance. Furthermore, the attack rate increased by 0.15% (p=0.005) per hour of co-travel time.

Using whole-genome sequencing of SARS-CoV-2 clinical samples during a nosocomial outbreak of COVID-19 in Dublin, Ireland, Lucey et al. reported that the majority of infections were among patients who required extensive and prolonged care by health care providers. The authors concluded that the likely mode of transmission from health care workers to patients was through respiratory droplets and close contact, rather than airborne transmission.

The reproductive number ($R_0$) is less suggestive of airborne spread, as airborne infections tend to have a higher $R_0$. For example, in a systematic review by Guerra et al., the $R_0$ for measles in the pre-vaccine era was 6.1–27.0, compared to the range of $R_0$ (2–3) reported for COVID-19.

**Evidence for distance travelled by respiratory droplets:**

Researchers have demonstrated the propulsion of respiratory droplets up to 2 m, and in a study by Guo et al., respiratory droplets were found on the floor up to 4 m away from a patient. A systematic review of studies assessing the horizontal distance travelled by respiratory droplets found that droplets could travel up to 8 m.

**Airborne Transmission**

Respiratory virus transmission occurs on a spectrum from larger droplets that spread at close range to smaller droplets (or aerosols) that have the potential to be infectious over longer distances (i.e. >2 m) and may be suspended for longer periods of time (typically hours). As summarized above, current evidence supports that SARS-CoV-2 transmission is predominantly through close, unprotected contact, which supports larger droplet spread. However, under conditions of poor ventilation or with recirculation of unfiltered and untreated air, aerosols may accumulate in sufficient quantities to become infectious and transmission via inhalation is plausible based on the emerging literature. Further evidence regarding the quantity of viral particles required to cause infection is needed. There is no evidence at this time of transmission over long distances through the air (such as through air ducts). The term “airborne transmission” has special meaning in public health, for infection prevention and control purposes, and in health care settings. This term is typically reserved to describe infections efficiently transmitted by small droplets and particles suspended in the air over long distances and persisting in the air for long periods (see Appendix for size designations). Airborne pathogens typically require specialized engineering controls to prevent spread (e.g. negative-pressure isolation rooms and specific personal protective equipment (PPE) such as respirators). However, the historical dichotomy of airborne vs non-airborne pathogens used in health care settings is likely imprecise. Infectious pathogens can be considered on a spectrum of efficiency for airborne transmission classified as obligate (infection only occurs via aerosols), preferential (aerosols predominate), or opportunistic (non-airborne transmission is most common but aerosols may transmit under favorable conditions). Current evidence supports SARS-CoV-2 as an opportunistic airborne pathogen.

A commentary by Morawska and Milton appealed to the medical community to recognize the potential for airborne transmission, based on experimental evidence that small respiratory droplets (or aerosols)
could be inhaled. Another commentary by Klompas et al. discussed how the balance of currently available evidence does not support long-range aerosol transmission as the dominant mode of COVID-19 transmission. While aerosols are reported by Stadnytskyi et al. to be produced during activities such as speaking, breathing and coughing, it is not clear what role aerosols have in transmission for distances greater than 2 m, as viable SARS-CoV-2 has only once been detected during air sampling. The role of these aerosols has been suggested in a modelling study by Chen et al. to be most important for transmission in close proximity (<2 m).

As discussed in the Droplet and Contact Transmission section, household secondary attack rates are more consistent with primary transmission through respiratory droplets when people are in close contact with one another, rather than airborne transmission. There is emerging evidence that opportunistic aerosol transmission occurs under the right combination of conditions (i.e. poorly ventilated space with sufficient quantity of infectious virus produced). However, as discussed above, this appears to be less frequent, and less efficient, when compared with direct close contact.

Environmental exposures, such as sunlight, may have significant effects on viability of SARS-CoV-2. Using a rotating drum experiment similar to other studies for viability of SARS-CoV-2, simulated sunlight (UVA/UVB) was applied to aerosolized virus through a window on the drum. Results indicated 90% inactivation of virus within 20 minutes.

**Experimental evidence of aerosol generation of SARS-CoV-2:**

In a study comparing SARS-CoV-2 and SARS-CoV-1, van Doremalen et al. reported that SARS-CoV-2 could be artificially aerosolized with a jet nebulizer and detectable for up to 3 h in a rotating metal drum. The half-lives of SARS-CoV-2 and SARS-CoV-1 were similar in aerosols with median estimates of the half-life of 1.1–1.2 h. While the van Doremalen et al. study concluded that aerosol transmission was possible, they did not demonstrate that it occurred (refer to the PHO Synopsis on this study for further details). Fears et al. drew similar conclusions through conducting a similar experiment.

Lee modelled the minimum sizes of aerosols emitted from an infected individual that could be expected to contain viral particles. Under certain assumptions, Lee estimated that the minimum sizes theoretically ranged from 0.4–42 μm; by using experimental data of virus in oral fluid, they estimated a range of 4.7–32 μm. Studies discussed by Lee detected virus by polymerase chain reaction (PCR) in much smaller aerosol sizes (<0.25–4 μm). The author reconciled differences in the modelled sizes and air-sampled sizes by acknowledging that aerosols evaporate to smaller sizes (which may take only seconds) and/or the possible range of virus in oral fluid can be higher than reported by the previous experiment used to inform this model. Lee also noted that the virus particles captured in those experiments may not be viable.

**Studies have not consistently detected viable SARS-CoV-2 in air samples:**

Multiple air sampling studies performed in proximity to confirmed COVID-19 cases were unable to detect any virus by PCR. Santarpia et al. was unable to culture virus from air samples collected outside of patient rooms. Similarly, Binder et al. reported that 3 PCR-positive air samples, collected at distances of 1–3.2 m from patients, were culture negative. Cheng V et al. sampled air at a high flow rate 10 cm from the chin of symptomatic and asymptomatic patients (n=6), with no viable virus detected by culture from collected air samples. One PCR-positive air sample was obtained during an endotracheal intubation within 10 cm of the patient’s head in a naturally ventilated room (window open
with fan attached); eleven other air samples near patients and 17 samples outside patient rooms and at nursing stations were PCR-negative.⁵⁰

Lednicky et al. used a prototype and commercial version of an air sampler and custom PCR probes for detection of SARS-CoV-2 in a patient room with two patients. One patient was discharged soon after sampling periods began and after receiving a negative PCR test.⁵¹ The remaining patient began experiencing respiratory illness two days prior to admission to the room. The results of the study include PCR-positive air samples following 3 h of sampling as well attempting viral cultures. Researchers positioned samplers 2–4.8 m from the recently symptomatic patient’s head. The ventilation unit provided 6 air changes/h, filtering air and treating air with UV irradiation before recycling the air. Estimates of virus per volume of air ranged from 6–74 tissue culture infective dose (TCID)₅₀ units/L of air. More studies quantifying viable virus, with details of the type of ventilation and patient characteristics as reported in this study, are needed to inform the gaps in understanding aerosol transmission.

Another study detected SARS-CoV-2 by PCR in 38.7% (14/31) of air samples from a London hospital in the United Kingdom (UK) during the first peak of their epidemic. However, Zhou et al. did not detect virus by culture, suggesting there may not be adequate virus present in air samples to cause transmission.⁵² Another study by Guo et al. detected SARS-CoV-2 by PCR in 35% (14/40) of air samples in an intensive care unit (ICU) and 12.5% (2/16) of air samples in the general ward that manages patients with COVID-19. 15 of 16 PCR-positive air samples were from within 2 m of patients, with 1/8 samples positive at 4 m away.³⁰ Ben-Shmuel et al. conducted limited sampling (generally one air sample per area) in rooms with ventilated and non-ventilated patients, at a nursing station, and in private and public areas of a quarantine hotel.⁵³ Positive air samples were detected in a room with a ventilated patient (n=1/1), at a nursing station (n=1/1), and in a quarantine hotel room (n=1/1). However, there were no positive air samples in rooms of non-ventilated patients (n=0/3), a donning area (n=0/1), and a public area of a quarantine hotel (n=0/1).

Kenarkoohi et al. detected SARS-CoV-2 in 1/5 samples from a ward containing intubated, severely ill patients, but did not find any positive air samples in other areas of the hospital such as wards with suspected, confirmed and mild patients.⁵⁴ In a series of distinct room types (two airborne infection isolation rooms [AIIR] with 15+ air changes per hour, an isolation room without negative pressure, and a shared cohort room) for patients admitted within 7 days of symptom onset, Kim et al. reported that 32 air samples were negative and 20 air samples from anterooms were also negative.⁵⁵

Chia et al., in an extended study of Ong et al., detected SARS-CoV-2 RNA by PCR in air samples collected within 1 m of patients in two of three AIIRs.⁵⁶ Lei et al. reported limited detection of SARS-CoV-2 virus by air sampling in open wards, private isolation rooms and bathrooms.⁵⁷

Further research is needed to reconcile differences in viral RNA detection and viral viability in air samples, despite positive samples found on the surfaces of ventilation units. Differences may be due to several factors, including: 1) air sampling devices were potentially not capable of maintaining viability of captured virus; 2) timing of air sampling varies by time since onset of symptoms, severity of disease, or viral load; and, 3) the conditions of ventilation (engineering controls) reducing concentrations of viral aerosols to undetectable levels.⁵⁹,⁶¹,⁵³

**Evidence for long distance spread of SARS-CoV-2 is uncommon:**

There were few reports that have identified long distance transmission of SARS-CoV-2. The minimal transmission to fellow passengers seated near individuals with COVID-19 on airplanes does not support an airborne transmission route.⁵⁸–⁶⁰ The airflows in an airplane cabin were modelled in a study
demonstrating how risk of infection may be restricted to certain areas in front and behind an infected passenger.61

In one case study, worshippers who were not wearing masks were exposed to a presymptomatic index patient for 100 minutes while on a bus.62 Twenty-four of 67 worshippers became infected, including several passengers seated beyond 2 m distance. Seven of 172 other worshippers attending the same event were positive for SARS-CoV-2. The bus containing the index patient was heated and air was recirculated without filtration. Infections occurred in individuals at either end of the bus and the index case was located roughly in the middle. Risk of infection was only moderately higher for individuals sitting closer to the index patient. The authors of this study postulate that the poor ventilation in the bus supports aerosols in this large transmission cluster; however, other routes of transmission such as close contact from movement within the bus or fomites could not be excluded.

An investigation by Lu et al. into a COVID-19 outbreak in a restaurant in Guangzhou, China involving three families sitting in close proximity for more than 1 hour concluded that the air conditioning (AC) ventilation likely contributed to transmission.63 In this scenario, there was between 53–73 min of contact between the presymptomatic index case and secondary cases. The location of a consistently running AC unit (the outlet and exhaust flanked the table of the index case) was in the airflow path of the secondary cases and was in an enclosed environment. No secondary cases occurred at adjacent tables that were outside of the likely “air column.” The furthest distance between index and secondary cases was approximately 3 m.

Recent outbreaks with detailed reporting are less likely to be explained completely by droplet or contact routes (Miller et al., Brlek et al.).64,65 In a choir group, 53 of 60 individuals (excluding the index patient) were confirmed or strongly suspected to have been infected during a 2.5 hour rehearsal in a main hall. Individuals who moved to another area of the building from the index case to practice for 45 min were less likely to have become infected than those who remained in the main hall for the full duration of the rehearsal.64,65 In another study, infection was documented from exposure in a squash court used by patrons after a recently symptomatic index patient had played for 1 hour. Two sets of patrons using the court after the index patient were also infected (up to 90 min later). Aerosol persistence in a poorly ventilated squash court, re-aerosolization of virus from the squash court floor due to rapid movement of players, or fomite transmission were possible routes of transmission. However, this case investigation strongly supports indirect transmission of SARS-CoV-2, most likely through persistence of aerosols in a poorly ventilated space.

In an outbreak in a nursing home, de Man et al. reported that the outbreak involved 81% (n=17) of residents and 50% (n=17) of health care workers. The authors concluded that AC units and a ventilation system that did not provide adequate air exchanges contributed to the outbreak.66 However, it should be noted that health care workers did not wear masks during non-patient care activities and the mobility and interaction between residents was not considered.

In a call center in South Korea, half of one floor of the office building experienced an outbreak in 94/216 employees.67 The outbreak description is limited in providing further detail because the index patient was not known, ventilation parameters were not reported (especially whether air circulation was shared on both sides of the building), and daily mingling habits were not described. A handful of infected individuals were detected on two other floors, but no outbreaks occurred in those areas and the infected individuals could not be linked to the outbreak.
The importance of ventilation is described in a modeling study by Jones, who suggested that exposure to inhalable particles are mostly (80%) experienced within close proximity to the patient. Even in rooms with high air exchanges, Tang et al.'s review of SARS-CoV-2 aerosols indicates that viral RNA copies can still be detected in air samples from patient rooms (1.8–3.4 viral RNA copies/m$^3$), toilet rooms (19 copies/m$^3$), and PPE doffing rooms (18–42 copies/m$^3$).

Airborne Transmission during AGMPs

There were no documented cases of airborne transmission of SARS-CoV-2 during AGMPs in the peer-reviewed literature we examined. We note the lack of transmission in these settings may be due to the appropriate use PPE during AGMPs, with few unprotected close-contact exposures.

Evidence for transmission of SARS-CoV-2 during AGMPs:

There is little evidence demonstrating AGMPs as a contributor to health care worker transmission. In a case-control study involving health care workers, Lentz et al. reported that while AGMPs were not associated with an increased risk of SARS-CoV-2 infection, respirator use during AGMPs lowered the risk of infection (adjusted OR: 0.4; 95% CI: 0.2–0.8; p=0.005).

While airborne transmission does not appear to be the predominant mode of transmission (i.e., such as in households and in routine patient care), medical procedures that generate aerosols may be associated with an increased risk of transmission. During the SARS outbreak in 2003, infections disproportionately occurred among healthcare workers, with those involved in AGMPs and manipulation of the airway (i.e., at the time of intubation) at greatest risk. An investigation into a nosocomial outbreak of SARS in Toronto concluded that the epidemiological links described in their investigation support the hypothesis that SARS-CoV-1 was transmitted primarily through respiratory droplets and direct contact, noting that transmission occurred during high-risk procedures (i.e. intubation) when only a surgical mask was utilized, in the absence of protective eyewear. Infected healthcare workers were no less likely to contract SARS-CoV-1 while wearing an N95 respirator (vs. surgical mask), suggesting that it may have been doffing (taking off) of PPE where transmission occurred. AGMPs do not appear to be a significant risk factor for SARS-CoV-2 transmission among health care workers, potentially related to improved health care worker precautions for AGMPs and/or the lower infectiousness of SARS-CoV-2 in the second week of illness (in contrast to SARS-CoV-1).

Fecal-oral (Feces, Wastewater) Transmission

While fecal-oral transmission of SARS-CoV-2 is possible, it is unclear the extent to which this transmission route plays in the epidemiology of COVID-19. The evidence supporting fecal-oral transmission was limited.

Researchers have documented angiotensin-converting enzyme 2 (ACE-2; proposed receptor used by SARS-CoV-2 to enter cells) receptor expression in gastrointestinal epithelial cells; SARS-CoV-2 infects these glandular cells, as evidenced by RNA detection and intracellular staining of viral nucleocapsid protein in gastric, duodenal and rectal epithelia. Gastrointestinal symptoms occur in about 9.5% of adults and children with COVID-19. Tissues in the oral cavity express ACE-2 receptors. SARS-CoV-2 RNA and live virus have been detected in the stool of patients with COVID-19. Given detection of infectious virus in stool and that virus can infect via the oral mucosa, fecal-oral transmission is possible.
Evidence for SARS-CoV-2 RNA detection and shedding in feces:

In systematic reviews, the mean prevalence of SARS-CoV-2-RNA-positive stool in patients with COVID-19 ranged from approximately 40% to 50% and viral RNA shedding in stool lasted longer than in nasopharyngeal (NP) swabs. In a systematic review and meta-analysis of 4,243 patients, Cheung et al. reported the prevalence of viral RNA in stool was 48.1% (95% CI: 38.3–57.9).82 In a meta-analysis by van Doorn et al., the pooled prevalence of viral RNA in stool or anal swabs was 51.8% (95% CI: 43.8%–59.7%); and fecal samples remained positive for a mean duration of 12.5 days after negative NP swabs in 282/433 (64%) of patients who had serial test results for both respiratory and GI specimens.83 A systematic review by Gupta et al. noted that 53.9% (291/540) of COVID-19 patients had viral RNA-positive fecal samples; duration of fecal shedding ranged from 1 to 33 days after negative NP swabs.84 Parasa et al. reported on a meta-analysis of 407 patients with COVID-19, where the prevalence of viral RNA-positive stool was 40.5% (95% CI: 27.4–55.1).85 In a meta-analysis, Wong MC et al. reported a pooled detection rate of viral RNA in fecal samples among patients was 43.7% (95% CI: 32.6–55.0).86

In studies detecting viral RNA in various clinical samples other than NP swabs, researchers more commonly detect viral RNA in stool of patients with COVID-19. In a systematic review of 569 patients by Roshandel et al., prevalence of viral RNA was higher in stool (39.5%) than blood (21.3%) and urine (8%).87 In another systematic review, Morone et al. reported the prevalence of viral RNA-positive stool (48.8%) was higher than positive blood (17.5%) and urine (16.4%) samples; median duration of viral shedding in stool was significantly longer than shedding in respiratory samples (19 days vs. 14 days; p<0.001).88 Comparing viral RNA detection in serum, urine and stool in 74 patients, Kim et al. reported a detection rate of 2.8% (9/323 samples), 0.8% (2/247) and 10.1% (13/129), respectively.89 The mean viral load was 1,210 ± 1,861, 79 ± 30 and 3,176 ± 7,208 copies/µL, respectively, and no viable virus was detected in cell cultures. In a review, Jones et al. noted that the abundance of viral RNA in urine (10^2–10^5 genome copies [gc]/ml) and feces (10^2–10^7 gc/ml) was lower than in NP swabs (10^5–10^11 gc/ml).90

In a study of 69 children, 86% had viral RNA-positive stool/rectal/anal swabs and the mean duration of viral shedding was 23.6 ± 8.8 days from symptom-onset.91 In a study of 69 patients with COVID-19, patients with positive fecal samples were significantly younger compared to patients with negative fecal samples (mean age: 43 vs. 52 years; p=0.003).92 Viral shedding in stool persisted for over 3 weeks since symptom-onset and the severity of COVID-19 was not associated with duration of viral shedding in stool.93,94

Kang et al. reported on an outbreak of COVID-19 in a high-rise apartment building in Guangzhou, China, where the proposed mode of transmission was through fecal aerosols via the pipes in the building.95 However, the authors did not demonstrate the exact mode of transmission; i.e., through direct contact or indirectly through inhalation of aerosolized virus or touching contaminated surfaces.

Environmental sampling in health care and non-health care settings detected viral RNA on toilets and other bathroom surfaces.43,55,96-99 While readily detected, it is not clear if the source of viral RNA in bathrooms was the result of respiratory droplets or from fecal contamination.

Evidence for live SARS-CoV-2 detection in feces:

Live virus has been cultured in stool samples of patients with COVID-19.100,101 In a systematic review, viable virus was detected in the stool of six out of 17 patients, where culturing of virus was attempted.83 It is important to note that the authors did not define positive and negative controls in these studies. While researchers detect live virus in feces, the extent of fecal-oral transmission in COVID-19 epidemiology is unclear.
Evidence for SARS-CoV-2 RNA in wastewater:
Viral RNA detection in wastewater systems in areas experiencing outbreaks; however, the risk of transmission through contaminated wastewater is low.\textsuperscript{102,103} In a study of treated and raw sewage in Germany, the authors detected viral RNA, but not viable virus.\textsuperscript{104} Where wastewater contaminates recreational or drinking water (especially in resource-limited countries), there is a theoretical risk of transmission; however, there is no documented transmission in these settings.\textsuperscript{105}

In a study of eight patients with COVID-19 in a densely populated area of Guangzhou, China, the postulated mode of transmission was through the fecal-oral route, initiated from contaminated sewage in street puddles (viral RNA-positive).\textsuperscript{106} In this study, there was an increased risk of infection when patients worked as cleaners/waste pickers, wore outdoor shoes inside their homes and cleaned dirty shoes. The authors did not confirm transmission via sewage in this study, as the authors did not detect viable virus from samples and they did not rule out other modes of transmission.

Conjunctival Transmission
To date, there is a low risk of COVID-19 infection through the conjunctiva.
Transmission through the ocular surface is a possible route of transmission of SARS-CoV-2 based on the detection of viral RNA in ocular samples of patients with COVID-19 and indirect evidence that eye protection decreases the risk of infection.\textsuperscript{107} The risk of tears or ocular secretions acting as a source of infection is low, given that only one study has successfully cultured viable virus in these samples.

Several studies have demonstrated the expression of ACE-2 and transmembrane serine protease 2 (TMPRSS2) receptors in the eye’s surface epithelium (i.e., conjunctiva, limbus and cornea) and corneal endothelium, indicating a potential entry point for SARS-CoV-2.\textsuperscript{108-111} The conjunctiva has been proposed as a possible site of initial infection, where it can spread to the upper respiratory tract via the nasolacrimal system.\textsuperscript{112} Deng et al. demonstrated that rhesus macaques developed mild disease after inoculation of the conjunctiva, providing further animal-study evidence of conjunctival transmission.\textsuperscript{113}

Evidence for conjunctival transmission:
In a case report, Lu et al. described a healthcare worker who became infected after caring for a patient with COVID-19; the health care worker was wearing an N95 respirator, but no eye protection.\textsuperscript{114} The health care worker developed eye redness and then pneumonia.

In a study of an ophthalmologist with COVID-19, 142 patients were exposed; however, only a single patient developed symptoms (but PCR negative), indicating the use of face shields, masks and performing hand hygiene prevented infection.\textsuperscript{115} In the meta-analysis by Chu et al., eye protection provided significant protection against coronavirus infections (unadjusted RR: 0.34; 95% CI: 0.22–0.52), suggesting that transmission through the conjunctiva was possible.\textsuperscript{116}

Fomite (Surfaces, Objects, Food) Transmission
SARS-CoV-2 can survive on a variety of surfaces, potentially leading to transmission via fomites; however, the evidence supporting fomite transmission of COVID-19 was limited and based primarily on studies of virus stability under laboratory-controlled conditions.
Evidence for fomite transmission of SARS-CoV-2:

From a detailed investigation, including whole genome sequencing, into an inter-facility outbreak of up to 135 nosocomial COVID-19 cases (including 88 staff and 47 patients) in South Africa, Lessells et al. concluded that a patient in the emergency department likely spread the infection to at least five hospital units, a local nursing home and an outpatient dialysis unit on campus. In this case, the authors concluded that indirect contact and fomite transmission were the predominant modes of transmission, facilitated by frequent patient movement between wards.

In an epidemiological and environmental study of two family clusters (n=5 patients) of COVID-19 in Guangzhou, China, Xie et al. reported potential transmission via contaminated surfaces. In this case, the proposed link between the two families was through nasal secretions, in which a patient had touched a contaminated elevator button. In this study, other modes of transmission cannot be ruled out and no viable virus was detected on surfaces (only viral RNA detection).

As mentioned previously, transmission in a squash court occurred in players that used the space after it was occupied by the index case for one hour. In this case, there is a possibility of aerosol persistence; however, transmission via fomites is possible (e.g., on high-touch surfaces).

Evidence for SARS-CoV-2 RNA detection on surfaces:

In health care settings, studies documented the presence of viral RNA on high-touch surfaces in the environment of symptomatic and asymptomatic patients with COVID-19 (especially medical equipment, phones, bed rails, door handles and toilets). In a hospital in Wuhan, China, Ye et al. reported that the most contaminated surfaces were self-service printers for patient use, keyboards and doorknobs. In Italy, researchers detected viral RNA on the external surface of Continuous Positive Airway Pressure (CPAP) helmets worn by COVID-19 patients; however, samples did not grow in viral culture. A study reported viral RNA on surfaces (keyboards, telephones and scanners) in a clinical microbiology laboratory testing COVID-19-patient respiratory samples. In a multicenter study in South Korea, contamination of surfaces was common, especially in places not adequately sanitized.

Cheng et al. reported that the median load of viral RNA on surfaces was $9.2 \times 10^2$ copies/mL (range: $1.1 \times 10^2$ to $9.4 \times 10^4$ copies/mL) and positivity rates on surfaces increased with increasing viral loads in clinical samples.

In non-healthcare settings (patient homes, work places), viral RNA has also been detected on surfaces (especially in bathrooms and bedrooms). In a study of 39 patients and 259 environmental samples from their homes (Guangzhou, China), surfaces most commonly contaminated with viral RNA were in the bathroom on high touch surfaces (toilets, door knobs, faucets).

Evidence for the detection of live SARS-CoV-2 on surfaces:

In most of the studies we examined, researchers failed to detect viable virus on surfaces or detection of viable virus was inconsistent. Ben-Shmuel et al. investigated the viability of SARS-CoV-2 from 97 samples from surfaces of patients. None of the samples grew in viral culture. In controlled experiments, virus viability on plastic and metal ceased after 4 days at ambient temperature (22°C) and decreases in virus viability negatively correlated with increasing temperature. Nonetheless, some studies indicate that under ideal conditions, SARS-CoV-2 remains viable on surfaces for several days.
Van Doremalen et al. compared surface stability of SARS-CoV-2 and SARS-CoV-1. The authors noted an exponential decay in virus titre for both viruses in all experimental conditions. At 40% relative humidity and 21°C–23°C, both SARS-CoV-2 and SARS-CoV-1 were detectable for up to 24 h on cardboard and up to 2–3 d on plastic and stainless steel. On copper, the authors did not find live SARS-CoV-2 and SARS-CoV-1 after 4 h and 8 h, respectively. The estimated median half-lives for SARS-CoV-2 on these surfaces were 0.7 h for copper, 3.5 h for cardboard, 5.6 h for stainless steel, and 6.8 h for plastic. While the van Doremalen et al. study concluded that fomite transmission is possible given detection of SARS-CoV-2 on a number of surfaces, they did not demonstrate that it occurs.

Riddell et al. tested the stability of SARS-CoV-2 under controlled conditions on seven surface types (stainless steel, plastic, paper bank notes, polymer bank notes, vinyl, cotton and glass). The authors concluded that infectious virus survived on non-porous surfaces for at least 28 d at 20°C and 50% relative humidity in the dark. In addition, virus titres decreased by 90% by 10 d post-inoculation at 20°C on all surfaces.

Chan et al. reported that at room temperature (20°C–25°C), SARS-CoV-2 in dried form or solution remained viable 3–5 d and 7 d, respectively; virus remained viable in solution or dried for 14 d at 4°C and about 1 d at 37°C. SARS-CoV-2 was detected at pH 4 to pH 11 for several days.

Chin et al. investigated the surface stability of SARS-CoV-2 at 22°C and 65% relative humidity. The authors did not detect infectious virus on printing and tissue paper 3 h after inoculation. Infectious virus was no longer present on glass or paper money by day 4 and on day 7 for plastic and stainless steel. The authors state, “The virus is highly stable at 4°C, but sensitive to heat. At 4°C, there was about a 0.7 log-unit reduction of infectious titre on day 14. With the incubation temperature increased to 70°C, the time for virus inactivation was reduced to 5 min. SARS-CoV-2 can be highly stable in favourable environments, but it is also susceptible to standard disinfection methods.”

**Evidence for food-borne transmission of SARS-CoV-2:**

To date, there is no evidence for food-borne transmission of SARS-CoV-2. No peer-reviewed studies investigated SARS-CoV-2 survival or detection on food and no peer-reviewed studies reported on infection through eating contaminated food. There is likely a risk of transmission from droplet or close contact during eating (from an infectious person); in addition, there is a possibility of fecal-oral transmission during eating with contaminated utensils.

Several studies have identified viral RNA on food preparation surfaces and utensils, which could potentially be a source of infection through the oral mucosa; however, the contribution of this mode of transmission is unknown. In a study of surfaces in health care settings, researchers have detected viral RNA on food preparation areas. Liu et al. reported the detection of viral RNA on wooden chopsticks handled by asymptomatic and presymptomatic patients with COVID-19.

**Vertical (Intrauterine) Transmission**

To date, there is growing evidence supporting vertical transmission, specifically intrauterine transmission, of SARS-CoV-2; however, the degree to which this mode of transmission occurs is unclear.

In a commentary, Schwartz et al. proposed that confirming vertical, intrauterine transmission requires detection of SARS-CoV-2 in chorionic villous cells using immunohistochemistry or in situ hybridization. Early onset of COVID-19 or detection of viral RNA soon after birth in neonates, along with immunological response in neonates and RNA-positive swabs of whole placenta are not sufficient to confirm
intrauterine transmission. In addition, vertical transmission would require the detection of viral RNA in umbilical cord tissue or blood.

**Evidence against vertical transmission of SARS-CoV-2:**

In five systematic reviews and meta-analyses, ranging from 87 to 1,316 births, there were SARS-CoV-2 RNA-positive newborns but no evidence of vertical transmission.\(^{132-136}\) In a systematic review of 1,125 mothers and 1,141 newborns, Dhir et al. concluded that the majority of infections in newborns occurred in the post-partum period (41/45; 4 infections were reported as congenital).\(^{137}\)

In a multicenter observational cohort study of 242 pregnant women in Spain, Marin Gabriel et al. found no evidence of vertical transmission in newborns.\(^{138}\) Yan et al. reported no vertical transmission in a series of 99 mothers with COVID-19, in which no children (n=100) tested positive.\(^{139}\) Liu et al. reported no vertical transmission after delivery in 19 mothers with COVID-19; neonates tested negative by PCR (throat swab, urine, feces); amniotic fluid and breast milk also tested negative by PCR.\(^{140}\)

**Evidence for post-partum infection (SARS-CoV-2 RNA not detected in placenta or umbilical cord):**

There are several studies where newborns tested positive (viral RNA, antibodies) soon after birth under strict infection control and prevention precautions; however, testing of chorionic villous cells or umbilical cord were negative or not performed.\(^{141-148}\) In a systematic review of 275 pregnant women with COVID-19 and 246 neonates, the testing of additional samples for viral RNA did not produce positive samples (cord blood, n=30; amniotic fluid, n=24; cervical/vaginal fluids, n=7; placenta, n=6).\(^{149}\)

Kirtzman et al. reported a case of probable vertical transmission of SARS-CoV-2 in a neonate born to a mother who tested positive for viral RNA by PCR on NP swab and put on airborne, droplet and contact precautions.\(^{150}\) The baby was born by semi-urgent Caesarean section and placed in a resuscitator 2 m away from the mother. The NP swab was positive for viral RNA at birth and on day 2 and 7. Neonatal plasma was viral RNA-positive on day 4 and on day 7 in stool. However, viral RNA was not detected by PCR on the umbilical cord tissue and cord blood was not available for testing.

Knight et al. report the results from a prospective national population-based cohort study using the UK Obstetric Surveillance System, which included 427 pregnant women admitted to hospital with COVID-19.\(^{151}\) Twelve (5%) of 265 infants tested positive by PCR for viral RNA, six within 12 h of birth. The authors did not attempt viral detection on the umbilical cord blood, placenta or vaginal secretions and did not describe infection prevention and control practices after birth.

**Evidence for vertical transmission of SARS-CoV-2:**

Using immunofluorescence, Taglauer et al. examined the location of SARS-CoV-2 spike glycoprotein (CoV2 SP) and two viral entry proteins (ACE-2, TMPRSS2) in placentas of 15 COVID-19-positive mothers and 10 COVID-19-negative mothers.\(^{152}\) CoV2 SP and ACE-2 were localized in the outer syncytiotrophoblast layer placental villi. However, several other studies report that the expression of ACE-2 and TMPRSSR in the placenta is low.\(^{153,154}\)

In a systematic review and meta-analysis of 122 neonates, Raschetti et al. reported that 5.7% of infections were confirmed as congenital, 4.9% were probable congenital infections and 1.6% were possible congenital infections.\(^{155}\)

Patanè et al. found viral RNA on the fetal side of the placenta in two mothers infected with COVID-19.\(^{156}\) Both children were also positive by PCR from NP swabs taken at birth. Hosier et al. analyzed the
placenta from a woman in her second trimester with symptomatic COVID-19 infection, complicated by preeclampsia and placental abruption. Hosier et al. detected viral RNA predominantly in the syncytiotrophoblast cells at the maternal-fetal interface of the placenta. Additionally, Zhang et al. reported virus in syncytiotrophoblast cells, atrophic endometrial glandular epithelium and subchorionic plate (Langhan’s fibrinoid) through in situ hybridization (2/53 placentas).

**Breastfeeding (Breast Milk) Transmission**

Currently, there is no evidence to support mother-to-child transmission of COVID-19 through breast milk. Researchers inconsistently detect SARS-CoV-2 RNA in breast milk, with no evidence of live virus in breast milk. There have been no documented cases where breast milk is the suggested mode of transmission to an infant.

During breastfeeding, an infected mother can transmit COVID-19 to the child through respiratory droplets and close-contact transmission. In a systematic review and meta-analysis, Raschetti et al. reported that close contact of mother and child in the first 72 hours of life increased the risk of infection in the child (aOR: 6.6; 95% CI: 2.6–16.0; p<0.0001), while breastfeeding did not (aOR: 2.2; 95% CI: 0.09–1.18; p=0.15).

In experiments that inoculated breast milk with live SARS-CoV-2, Holder pasteurization inactivated the virus; therefore, suggesting donated breast milk that is pasteurized may be safe for recipient children and care providers.

**Evidence for SARS-CoV-2 RNA detection in breast milk:**

The majority of the literature agrees that there is no transmission of SARS-CoV-2 through breast milk and the benefits of breastfeeding newborns far outweigh any risks of infection. In most studies of mothers with COVID-19, breast milk was negative for viral RNA by PCR. While uncommon, there are case reports of mothers with viral RNA-positive breast milk; however, there were no detections of viable virus from breast milk. In a living systematic review, Centeno-Tablante et al. reported that 9 of 68 breast milk samples were viral RNA-positive, but concluded that COVID-19 transmission did not occur through breast milk.

A case report detected viral RNA in the breast milk of a breastfeeding mother with COVID-19. The breastfed child developed symptoms one day after his mother, at which time he tested positive by NP swab. The transmission route in this case could not be established.

Groß et al. report on a study of two women who tested positive for viral RNA by PCR after birth and were breastfeeding. Breast milk was viral RNA-positive in one of the two women at 10–13 days after birth. The authors did not attempt to culture the virus. Both infants tested positive for viral RNA (at day 8 and 11), but it is unknown if breastfeeding led to the infection in one of the infants, as the two women and infants had shared a room for some time after delivery.

**Evidence for SARS-CoV-2 antibodies in breast milk:**

Antibodies to SARS-CoV-2 have been detected from breast milk. In a study of 14 mothers with COVID-19, Gao et al. did not detect viral RNA in breast milk; however, three out of four mothers had breast milk with IgG and IgM antibodies. In another immunological study of 18 women with COVID-19, both IgG and IgA were detected in all 37 of breast milk samples.
Bloodborne (Blood, Blood Products, Organs) Transmission

While SARS-CoV-2 RNA has been detected in the blood of patients with COVID-19, all systematic reviews and studies indicated that the risk of bloodborne or organ transplant transmission is exceedingly low. Compared to upper respiratory samples, the detection of viral RNA in blood and blood products is relatively uncommon and, to our knowledge, there has been no detection of viable virus from these sources.

Evidence for SARS-CoV-2 RNA detection in blood:

Several studies have reported detection of viral RNA, in either the plasma or serum of patients with COVID-19. In Germany, viral RNA was not detected in whole blood or serum of 18 asymptomatic and symptomatic patients; however, viral RNA (low-level RNA: 179 copies/mL) was detected in the plasma of one patient. In a systematic review including 1,348 recovered patients, 17.5% of blood samples were positive for viral RNA; however, no viable virus was cultured.

Evidence against blood-borne transmission:

Several case reports and case series indicate the risk of SARS-CoV-2 transmission in blood products is exceedingly low. In a review, Kiely et al. noted that bloodborne transmission is only a theoretical possibility and that a blood phase for COVID-19 infection is brief, uncommon and usually associated with severe disease. In an immunocompromised child, COVID-19 did not develop after platelet transfusion from an asymptomatic donor with COVID-19. In France, low levels of viral RNA were detected in three blood products (pathogen-reduced platelet concentrate, plasma, red blood cell units) from asymptomatic COVID-19-positive donors; none of the four recipients developed disease even though they all had immune system compromise. In the French study, positive plasma samples did not grow virus in culture attempts. Dres et al. reported no transmission of SARS-CoV-2 through extracorporeal membrane oxygenation and dialysis membranes.

No studies have documented transmission of SARS-CoV-2 through organ transplantation. While research has not demonstrated permanent damage to non-lung organs, the consensus is that active COVID-19 infection in donors (living or deceased) is a contraindication for organ donation. Hong et al. reported a possible infection in a liver donor recipient, in which the donor was infected at time of donation; however, transmission may have been through direct close contact.

Sexual (Semen, Vaginal Secretions, Urine) Transmission

Sexual transmission may occur through direct contact and through respiratory droplets. The risk of transmission via semen or vaginal secretions is low and the evidence supporting transmission via semen or vaginal secretions was limited.

Based on viral detection in feces, some have proposed possible transmission of SARS-CoV-2 through certain sexual behaviours involving oral-anal contact. In addition, the detection of viral RNA and live virus detected in the saliva of COVID-19 patients represents a potential mode of transmission during sex or intimate contact. Jing et al. reviewed the literature on ACE-2 expression in the female reproductive system and noted expression of ACE-2 receptors in the vagina. ACE-2 receptors are also present in testes (i.e., spermatogonia, Leydig and Sertoli cells). While receptors for SARS-CoV-2 are present in reproductive organs, currently there is no evidence for sexual transmission. There was no evidence for the detection of live virus in semen or vaginal secretions.
Evidence for SARS-CoV-2 RNA detection in semen and vaginal secretions:

To date, most studies have failed to detect viral RNA in semen or vaginal secretions in patients with COVID-19 patients. In a study of 23 male patients with active infection or recovering from infection, Guo et al. did not detect viral RNA in semen samples. Similarly, a study of nine males recovering from mild COVID-19 infection did not show evidence of viral shedding in semen.

Li et al. reported that 15.8% (6/38) of male COVID-19 patients had viral RNA present in their semen. The authors collected semen samples from two clinically recovered patients and four patients at the acute stage of infection. In the Li et al. study, the authors detected viral RNA up to 16 d after the onset of symptoms. Massarotti et al. hypothesized that viral RNA detections in semen are due to viral RNA-contamination by patient urine.

Evidence for SARS-CoV-2 RNA detection in urine:

Researchers report detection of viral RNA in urine; however, the risk of transmission via urine is low. We are only aware of one instance where infectious virus was isolated from the urine of a patient with COVID-19.

In a systematic review and meta-analysis, Roshandel et al. reported that 8.1% of (46/569; see Table 3 in paper) patients showed viral RNA shedding in urine (compared to 42.1% [210/499] for stool and 21.3% [100/469] for stool; see Figure 2 in paper) and viral RNA shedding in urine increases with disease severity. In a systematic review, 16.4% (60/366) of patients were positive for viral RNA in urine. In another systematic review of 549 patients, 6.9% showed evidence of viral RNA in their urine; however, culturing attempts were not successful. In a study of 74 patients hospitalized with COVID-19, Kim et al. found that 0.8% (2/247) of urine samples were positive for viral RNA (viral load: 79 ± 30 copy/µL; compared to 3,176 ± 7,208 copy/µL in stool); however, no viable virus was cultured.

Zoonotic transmission

Evidence for zoonotic transmission from companion, domestic and wild animals to humans was limited. Most of the evidence to date indicated that non-human animals are more at risk of infection from humans, especially companion and domestic animals. Further research is needed to identify potential reservoirs of SARS-CoV-2 and what risk they pose to humans and animals.

Early research revealed SARS-CoV-2 is a close relative of SARS-CoV-1 and MERS-CoV, and all are βCoVs that originated from bats (Rhinolophus species). Natural infection of animals with SARS-CoV-2, were all exposed to symptomatic humans. Infected animals include companion animals (domestic dogs [Canis lupus], domestic cats [Felis catus], farmed animals (American mink [Neovison vison], and zoo animals (lions [Panthera leo], tigers [Panthera tigris]).

Evidence for animal-to-human and animal-to-animal transmission:

Currently, the intermediate source of the initial COVID-19 infections in humans is unknown and the risk of transmission from animals to humans is low.

Malayan pangolins (Manis javanica) have been postulated as the intermediate host based on the presence of viruses closely related to SARS-CoV-2; however, this hypothesis has not been confirmed. Recently, Freuling et al. reported that raccoon dogs (Nyctereutes procyonoides) are susceptible to SARS-CoV-2 infection and may represent an important intermediate and reservoir host.
this study infected raccoon dogs through the intranasal route, which led to animal-to-animal transmission through direct contact, with high-level viral shedding with mild disease. Raccoon dogs are widespread in China and raised for their fur. It is important to note that there are no reports of SARS-CoV-2 natural infection in raccoon dogs.

In the Netherlands, there was evidence that COVID-19 transmission occurred from an infectious American mink to human.\textsuperscript{208} It should be noted that in most circumstances, transmission of SARS-CoV-2 involving animals is human-to-animal or animal-to-animal.\textsuperscript{203} In a laboratory experiment, ferrets can transmit the virus to other ferrets through respiratory droplets and direct contact,\textsuperscript{209} and potentially via small aerosols.\textsuperscript{210}

In a laboratory experiment, dogs and cats were susceptible to COVID-19; however, neither developed clinical disease.\textsuperscript{203,211} Cats transmitted the virus to other cats through close contact. Cats shed virus for 5 days post infection; however, there was no viral shedding in dogs. Authors noted oral and nasal viral shedding 7 days after exposure in two in-contact cats. Therefore, there is a possibility that transmission could occur from cats to humans. In addition, Shi et al. reported that experimental exposure in cats resulted in subclinical and symptomatic infections, and juvenile cats were at a higher risk of severe infection or death.\textsuperscript{212}

**Evidence for human-to-animal transmission (reverse zoonosis):**

The first documented instance of human-to-animal transmission occurred between an infected person in Hong Kong and their companion dog, soon after there was a report of human-to-cat transmission in Hong Kong.\textsuperscript{205} There is evidence that human-to-dog transmission may be limited due to cross-reaction of SARS-CoV-2 and canine respiratory coronavirus (CRCoV), providing some immunological cross-protection.\textsuperscript{213} The most commonly reported human-to-animal transmission has involved domestic cats, where most cats have a reported close contact with a confirmed human case of COVID-19.\textsuperscript{203,214} In Wuhan, China, 14.7% (15/102) of cats seroconverted to SARS-CoV-2 early during the pandemic.\textsuperscript{215}

Several researchers have highlighted the need to monitor wild animals, to ensure that reverse zoonosis does not occur (human-to-animal transmission). Olival et al. reported that there is a risk of immunologically naïve North American bats acquiring SARS-CoV-2.\textsuperscript{216} Researchers also demonstrated that deer mice (\textit{Peromyscus maniculatus}) are susceptible to infection and are potential reservoirs of SARS-CoV-2 in North America.\textsuperscript{217}

To date, laboratory studies indicate that domestic ducks (\textit{Anas platyrhynchos domesticus}), chickens (\textit{Gallus gallus domesticus}) and pigs (\textit{Sus scrofa}) were not susceptible to SARS-CoV-2.\textsuperscript{212,218}

Other susceptible animals, used in laboratory experiments or as animal models, include ferrets (\textit{Mustela putorius}), fruit bats (\textit{Rousettus aegyptiacus}), rhesus monkeys (\textit{Macaca mulatta}) and Syrian hamsters (\textit{Mesocricetus auratus}).\textsuperscript{212,219}

**Conclusions**

Transmission of SARS-CoV-2 occurs predominantly through respiratory droplets during close (<2 m), unprotected contact. Airborne transmission over longer distances (>2 m) through the inhalation of small respiratory droplets or aerosols is less common, but possible under certain conditions such as prolonged exposure in a poorly ventilated space.
Relatively uncommon routes of transmission of SARS-CoV-2 include conjunctival, vertical, fecal-oral, fomite and zoonotic. These routes of transmission are possible; however, their contribution to COVID-19 epidemiology is unclear. While modes of transmission such as through semen, breast milk or urine are theoretically possible, the probability of these occurring is exceedingly low.

PHO will continue to monitor the scientific evidence on transmission routes of COVID-19, updating this document as necessary.


COVID-19 Routes of Transmission – What We Know So Far


Jones DL, Baluja MQ, Graham DW, Corbishley A, McDonald JE, Malham SK, et al. Shedding of SARS-CoV-2 in feces and urine and its potential role in person-to-person transmission and the


Appendix A. Glossary of Terms for COVID-19 Routes of Transmission

Advisory

The glossary below contains definitions that may be changing with the understanding of evidence. Definitions may be different from how the same terms are used in other contexts or even seen as controversial due to different use within the same context by different organizations. Therefore, these definitions are provided to support the understanding of the COVID-19 – What We Know So Far About... Routes of Transmission document. This glossary is not exhaustive and may be updated with new terms or revised at any time.

Key Terms

**Airborne transmission:** Transmission of infection occurring due to the inhalation of aerosols that have remained suspended for a long period of time or have been suspended on air currents over long distances.

**Air sampling for virus:** Collection of volumes of air by a device to determine if aerosols may contain virus. Collection can vary by aerodynamic size captured, duration of collection, volume per second collected, and media on which samples deposit. Air samples can then be tested by molecular methods and/or viral culture.

**Aerosol:** Aerosols are defined by National Institute for Occupational Safety and Health (NIOSH) as a suspension of particles (solids) or droplets (liquids) in the air. The diameter of microorganism-containing aerosols relevant to inhalation ranges from 0.01 to 100 μm. Discussion of respiratory infections focus on droplets rather than particles because the sources of infectious aerosols are assumed to be from respiratory mucosa or epithelium, which will be droplets (liquids) that contain infectious biological material. Droplets >100μm are too large to be suspended in the air, and are therefore not considered aerosols. Droplets generally lose mass while suspended in air as aerosols due to evaporation of volatile components or water. The droplets that result from the process of evaporation are often referred to as droplet nuclei. The final size of a droplet will depend on a variety of environmental factors.

**Aerosol generating medical procedures:** Aerosol generating medical procedures (AGMPs) are defined as medical procedures that result in the production of aerosols that create the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route, and are epidemiologically associated with an increased risk of acquisition of infection.

**Contact transmission:** Transmission of infection through direct contact.

**Direct transmission:** Transmission of infection through contact or droplet transmission.

**Droplet transmission:** Transmission of infection occurring due to impaction of large droplets (usually >100 um) that are too large to be suspended in air for long durations. Infection may follow by direct impaction onto mucosal surfaces (mouth, eyes, nose), or contaminate a person’s body/clothing which then makes direct or indirect contact with susceptible surfaces (e.g., mucosal surfaces for COVID-19).
**Indirect transmission:** Includes any mode of transmission where direct contact or droplet transmission is not involved (e.g., fomite transmission, airborne transmission, and vectors).

**Fomite/Fomite transmission:** Objects that may become contaminated with microorganisms and serve as vehicles of transmission.

**Polymerase Chain Reaction (PCR):** A molecular method used to amplify nucleic acids. If nucleic acids of the microorganism of interest is present in a sample, then PCR can be used for the identification of that microorganism. This method cannot determine whether or not the microorganisms detected are viable.

**Viral culture:** Viral culture is used to determine whether a sample containing virus is capable of replication. Replication is a surrogate measure for inducing infection. Other methods to detect virus in a sample such as PCR cannot determine the viability of the organism in the sample. A sample is applied to a susceptible culture of cells and incubated up to a few weeks to detect morphological changes such as plaques that would indicate the presence of a viable virus.

**Appendix References**


Appendix B. MEDLINE Search Strategy

Search results reporting

DATABASES SEARCHED

<table>
<thead>
<tr>
<th>Database</th>
<th>Date searched</th>
<th>Records</th>
<th>Duplicates removed by database</th>
<th>Remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDLINE</td>
<td>10/14/2020</td>
<td>2641</td>
<td>330</td>
<td>2311</td>
</tr>
</tbody>
</table>

RECORDS TOTALS

<table>
<thead>
<tr>
<th>Records source</th>
<th>Records</th>
</tr>
</thead>
<tbody>
<tr>
<td>Records identified through database searching</td>
<td>2641</td>
</tr>
<tr>
<td>Duplicates removed by database</td>
<td>330</td>
</tr>
<tr>
<td>Duplicates removed by bibliographic management software</td>
<td>11</td>
</tr>
<tr>
<td>Total records after duplicates removed</td>
<td>2300</td>
</tr>
</tbody>
</table>

Search strategies

MEDLINE

Ovid MEDLINE(R) ALL <1946 to May 29, 2020>

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
<th>Results</th>
<th>Concept</th>
</tr>
</thead>
</table>
| 1 | ("2019 corona virus" or "2019 coronavirus" or "2019 ncov" or "corona virus 19" or "corona virus 2019" or "corona virus disease 19" or "corona virus disease 2019" or "corona virus epidemic*" or "corona virus outbreak*" or "corona virus pandemic*" or "coronavirus 19" or "coronavirus 2019" or "coronavirus 2019" or "coronavirus disease 19" or "coronavirus disease 2019" or "coronavirus epidemic*" or "coronavirus outbreak*" or "coronavirus pandemic*" or "covid 19" or "covid 2019" or "new corona virus" or "new coronavirus" or "novel corona virus" or "novel coronavirus" or "novel human coronavirus" or "sars coronavirus 2" or "sars cov 2" or "sars cov2" or "sars like coronavirus" or "severe acute respiratory syndrome corona virus 2" or "severe acute respiratory syndrome coronavirus 2" or "severe specific contagious pneumonia" or "wuhan corona virus" or "wuhan coronavirus" or 2019ncov or covid19 or covid2019 or ncv or sarscov2) or ((novel or Wuhan or China or Chinese or "seafood

COVID-19 Routes of Transmission – What We Know So Far 39
<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
<th>Results</th>
<th>Concept</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Disease Transmission, Infectious/ or Virus Shedding/ or tm.fs. or (transmi* or spread* or infectivity or (infect* adj3 route*) or excret* or shed*).kf,kw,ti. or (transmi* or spread* or infectivity or (infect* adj3 route*) or excret* or shed*).ab. /freq=2</td>
<td>493440</td>
<td>Transmission</td>
</tr>
<tr>
<td>3</td>
<td>(route* or mode or modes or &quot;non-respiratory&quot; or nonrespiratory or (transmission adj3 (dynamics or risk or potential))).kf,kw,ti.</td>
<td>92893</td>
<td>Route</td>
</tr>
<tr>
<td>4</td>
<td>Bodily Secretions/ or Body Fluids/ or Sneezing/ or Cough/ or (droplet* or ((body or bodies or lung* or mouth* or nose*) adj3 (fluid* or secretion* or secrete or discharge*)) or cough* or sneez*).kf,kw,ti.</td>
<td>74516</td>
<td>Droplet</td>
</tr>
<tr>
<td>5</td>
<td>exp Parents/ or Family/ or Grandparents/ or Housing/ or Public Housing/ or Siblings/ or Spouses/ or (&quot;close contact*&quot; or &quot;communal living&quot; or &quot;direct contact*&quot; or &quot;flat mate*&quot; or &quot;personal residence*&quot; or &quot;physical contact*&quot; or accommodation* or apartment* or brother* or cohabit* or &quot;co-habit*&quot; or coliving or &quot;co-living&quot; or commune or communes or condo* or contacts or domicile* or dwelling* or familial or family or families or father* or flatmate* or grandparent* or ((home or homes) not &quot;stay at home order*&quot;) or hous* or husband* or intrafamilial or mother* or parent or parents or relatives or roommate* or &quot;room mate*&quot; or sibling* or sister* or spouse* or wife or wives).kf,kw,ti.</td>
<td>688458</td>
<td>Contact</td>
</tr>
<tr>
<td>6</td>
<td>Conjunctiva/ or Conjunctivitis, Viral/ or Conjunctivitis/ or Eye/ or Tears/ or (conjunctiv* or eye or eyes or ocular or tear or tears).kf,kw,ti.</td>
<td>212437</td>
<td>Conjunctiva</td>
</tr>
<tr>
<td>7</td>
<td>Air/ or Air Microbiology/ or Air Pollution, Indoor/ or Inhalation Exposure/ or Exhalation or Air Ambulances/ or Aircraft/ or Ventilation/ or (air or airborne* or aircraft* or airplane* or ((building* or room* or office*) adj3 circulat*) or exhal* or flight or flights or HVAC or inhal* or plane or planes or vent or vents or &quot;ventilation system*&quot; or duct*).kf,kw,ti.</td>
<td>282916</td>
<td>Airborne</td>
</tr>
<tr>
<td>8</td>
<td>Aerosols/ or ((Disease Transmission, Infectious/ or Coronavirus Infections/tm or Pneumonia, Viral/tm) and (Intubation/ or Intubation, Intratracheal/ or Cardiopulmonary Resuscitation/ or Suction/ or Bronchoscopy/ or exp Surgical Procedures, Operative/ or surgery.f.s. or Autopsy/ or Sputum/ or exp Positive-Pressure Respiration/ or Oxygen Inhalation Therapy))/ or aerosol*.kf,kw,ti. or ((transmi* or spread* or infect*) and (nebuliz* or nebulis* or intubat* or ((cardiopulmonary or &quot;cardio-pulmonary&quot;) adj3</td>
<td>59726</td>
<td>Aerosol-Generating Procedures</td>
</tr>
<tr>
<td>#</td>
<td>Searches</td>
<td>Results</td>
<td>Concept</td>
</tr>
<tr>
<td>---</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>9</td>
<td>Fomites/ or Health Facility Environment/ or Patients' Rooms/ or Disease Reservoirs/ or exp Textiles/ or Clothing/ or Glass/ or Plastics/ or Metals/ or Cell Phone/ or Computers, Handheld/ or Smartphone/ or fomite*.kf,kw,ti. or ((clean* or colonis* or coloniz* or contamina* or decay* or decontaminat* or detect* or disinfect* or distribut* or expos* or grow* or harbor* or harbour* or inactivat* or &quot;infection control&quot; or persist* or sanit* or stabilit* or surviv* or viab*) adj15 (bathroom* or bed* or carpet* or chair* or cloth* or counter or counters or curtain* or &quot;door handle**&quot; or &quot;door knob**&quot; or doorknob* or environment* or equipment or fabric* or faucet* or fixture* or floor* or furnish* or furniture* or glass* or gown* or handrail* or &quot;hand rail&quot;* or ipad* or iphone* or keyboard* or keypad* or &quot;key pad**&quot; or &quot;light switch**&quot; or linen* or material* or mattress* or metal* or phone* or plastic* or raling or railings or reservoir* or sink* or smartphone* or surface or surfaces or telephone* or textile* or tile* or toilet* or &quot;touch screen**&quot; or upholster* or wall* or washroom*)).kf,kw,ti.</td>
<td>400853</td>
<td>Fomites</td>
</tr>
<tr>
<td>10</td>
<td>Feces/ or Diarrhea/ or exp Gastrointestinal Diseases/ or (fecal or faecal or feces or stool or stools or diarrhea or diarrhoea or enterocolitis or gastrointestinal* or gastrointestin* or gastroenter*).kf,kw,ti.</td>
<td>1125779</td>
<td>Fecal-Oral</td>
</tr>
<tr>
<td>11</td>
<td>Blood-Borne Pathogens/ or Blood Safety/ or bl.fs. or (bloodborne or blood or BBI).kf,kw,ti.</td>
<td>2190148</td>
<td>Bloodborne</td>
</tr>
<tr>
<td>12</td>
<td>Sexually Transmitted Diseases/ or Sexually Transmitted Diseases, Viral/ or Semen/ or Semen Analysis/ or Vaginal Discharge/ or Vaginal Smears/ or (sexual* or semen or vagina*).kf,kw,ti.</td>
<td>213704</td>
<td>Sexual Transmission</td>
</tr>
<tr>
<td>13</td>
<td>Amniotic Fluid/ or Breast Feeding/ or exp Delivery, Obstetric/ or exp Parturition/ or exp Pregnancy/ or Fetal Blood/ or Fetus/ or Infant, Newborn/ or Infectious Disease Transmission, Vertical/ or Maternal Exposure/ or Maternal-Fetal Exchange/ or Milk, Human/ or Peripartum Period/ or Postpartum Period/ or Pregnancy Complications, Infectious/ or Pregnancy Complications/ or Pregnancy Outcome/ or Pregnancy, High-Risk/ or Pregnant Women/ or (&quot;amniotic fluid&quot; or &quot;breast feeding&quot; or &quot;breast milk&quot; or &quot;cord blood&quot; or &quot;fetal blood&quot; or &quot;human milk&quot; or &quot;in utero&quot; or ((infant* or baby or babies) and mother*) or birth* or breastfeeding or breastfeeding or breastmilk or fetal or fetus or foetal or foetus or gestation* or gestation* or infant* or intrapartum or intrapartum or maternal* or mother* or natal* or neonat* or newborn* or obstetric* or parturition or perinatal* or placenta* or placenta* or postnatal* or postpartum* or pregnan* or prenatal* or puerperal*</td>
<td>1928571</td>
<td>Vertical Transmission</td>
</tr>
<tr>
<td>#</td>
<td>Searches</td>
<td>Results</td>
<td>Concept</td>
</tr>
<tr>
<td>----</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>14</td>
<td>1 and 2 and 3</td>
<td>296</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>1 and 2 and 4</td>
<td>165</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>1 and 2 and 5</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>1 and 2 and 6</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>1 and 2 and 7</td>
<td>318</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>1 and 2 and 8</td>
<td>886</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>1 and 9</td>
<td>550</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>1 and 2 and 10</td>
<td>285</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>1 and 2 and 11</td>
<td>141</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>1 and 2 and 12</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>1 and 2 and 13</td>
<td>590</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24</td>
<td>3063</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>(&quot;2019 corona virus&quot; or &quot;2019 coronavirus&quot; or &quot;2019 ncov&quot; or &quot;corona virus 19&quot; or &quot;corona virus 2019&quot; or &quot;corona virus disease 19&quot; or &quot;corona virus disease 2019&quot; or &quot;corona virus epidemic*&quot; or &quot;corona virus outbreak*&quot; or &quot;corona virus pandemic*&quot; or &quot;coronavirus 19&quot; or &quot;coronavirus 2019&quot; or &quot;coronavirus 1992&quot; or &quot;coronavirus disease 19&quot; or &quot;coronavirus disease 2019&quot; or &quot;coronavirus epidemic*&quot; or &quot;coronavirus outbreak*&quot; or &quot;coronavirus pandemic*&quot; or &quot;covid 19&quot; or &quot;covid 2019&quot; or &quot;new corona virus&quot; or &quot;new coronavirus&quot; or &quot;novel corona virus&quot; or &quot;novel coronavirus&quot; or &quot;novel human coronavirus&quot; or &quot;sars coronaviruses 2&quot; or &quot;sars cov 2&quot; or &quot;sars cov2&quot; or &quot;sars like coronaviruses&quot; or &quot;severe acute respiratory syndrome coronavirus 2&quot; or &quot;severe acute respiratory syndrome coronavirus 2&quot; or &quot;severe specific contagious pneumonia&quot; or &quot;wuhan corona virus&quot; or &quot;wuhan coronaviruses&quot; or 2019ncov or covid19 or covid2019 or ncov or sarscov2 or ((novel or Wuhan or China or Chinese or &quot;seafood market&quot; or &quot;2019&quot; or &quot;outbreak&quot; or epidemic* or pandemic*) adj5 (coronavirus* or &quot;corona virus*&quot; or betacoronavirus* or &quot;beta coronavirus*&quot; or &quot;beta corona virus*&quot; or pneumonia* or SARS or &quot;severe acute respiratory syndrome&quot;) or ((coronavirus* or &quot;corona virus*&quot; or betacoronavirus* or &quot;beta coronavirus*&quot; or &quot;beta corona virus*&quot; or SARS or &quot;severe acute respiratory syndrome&quot;) adj5 pneumonia*) or &quot;coronavirus response&quot; or &quot;corona virus response&quot;).ti.</td>
<td>66947</td>
<td>COVID-19</td>
</tr>
<tr>
<td>27</td>
<td><em>Disease Transmission, Infectious/ or <em>Virus Shedding/ or <em>Coronavirus Infections/tm or <em>Pneumonia, Viral/tm or (transmi</em> or spread</em> or (infect</em> and route</em>) or excret* or shed*).ti.</td>
<td>183017</td>
<td>Transmission</td>
</tr>
<tr>
<td>28</td>
<td>26 and 27</td>
<td>2994</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>25 or 28</td>
<td>4832</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>limit 29 to yr=&quot;2020 -Current&quot;</td>
<td>4642</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>limit 30 to English</td>
<td>4539</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>(202006* or 202007* or 202008* or 202009* or 202010*).ez.</td>
<td>585088</td>
<td></td>
</tr>
<tr>
<td>#</td>
<td>Searches</td>
<td>Results</td>
<td>Concept</td>
</tr>
<tr>
<td>----</td>
<td>-----------------------------------------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>33</td>
<td>31 and 32</td>
<td>2802</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>limit 33 to (comment or editorial or news)</td>
<td>161</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>33 not 34</td>
<td>2641</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>remove duplicates from 35</td>
<td>2311</td>
<td></td>
</tr>
</tbody>
</table>
Citation


Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario’s government, public health organizations and health care providers. PHO’s work is guided by the current best available evidence at the time of publication.

The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

This document may be reproduced without permission for non-commercial purposes only and provided that appropriate credit is given to PHO. No changes and/or modifications may be made to this document without express written permission from PHO.

Public Health Ontario

Public Health Ontario is an agency of the Government of Ontario dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit publichealthontario.ca.