Transmission of SARS-CoV-2: implications for infection prevention precautions

Scientific brief

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This document is an update to the scientific brief published on 29 March 2020 entitled "Modes of transmission of virus causing COVID-19: implications for infection prevention and control (IPC) precaution recommendations" and includes new scientific evidence available on transmission of SARS-CoV-2, the virus that causes COVID-19.

Overview

This scientific brief provides an overview of the modes of transmission of SARS-CoV-2, what is known about when infected people transmit the virus, and the implications for infection prevention and control precautions within and outside health facilities. This scientific brief is not a systematic review. Rather, it reflects the consolidation of rapid reviews of publications in peer-reviewed journals and of non-peer-reviewed manuscripts on pre-print servers, undertaken by WHO and partners. Preprint findings should be interpreted with caution in the absence of peer review. This brief is also informed by several discussions via teleconferences with the WHO Health Emergencies Programme ad hoc Experts Advisory Panel for IPC Preparedness, Readiness and Response to COVID-19, the WHO ad hoc COVID-19 IPC Guidance Development Group (COVID-19 IPC GDG), and by review of external experts with relevant technical backgrounds.

The overarching aim of the global Strategic Preparedness and Response Plan for COVID-19(1) is to control COVID-19 by suppressing transmission of the virus and preventing associated illness and death. Current evidence suggests that SARS-CoV-2, the virus that causes COVID-19, is predominantly spread from person-to-person. Understanding how, when and in what types of settings SARS-CoV-2 spreads is critical to develop effective public health and infection prevention and control measures to break chains of transmission.

Modes of transmission

This section briefly describes possible modes of transmission for SARS-CoV-2, including contact, droplet, airborne, fomite, fecal-oral, bloodborne, mother-to-child, and animal-to-human transmission. Infection with SARS-CoV-2 primarily causes respiratory illness ranging from mild disease to severe disease and death, and some people infected with the virus never develop symptoms.

Contact and droplet transmission

Transmission of SARS-CoV-2 can occur through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions or their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings.(2-10) Respiratory droplets are >5-10 µm in diameter whereas droplets ≤5µm in diameter are referred to as droplet nuclei or aerosols.(11) Respiratory droplet transmission can occur when a person is in close contact (within 1 metre) with an infected person who has respiratory symptoms (e.g. coughing or sneezing) or who is talking or singing; in these circumstances, respiratory droplets that include virus can reach the mouth, nose or eyes of a susceptible person and can result in infection. Indirect contact transmission involving contact of a susceptible host with a contaminated object or surface (fomite transmission) may also be possible (see below).

Airborne transmission

Airborne transmission is defined as the spread of an infectious agent caused by the dissemination of droplet nuclei (aerosols) that remain infectious when suspended in air over long distances and time.(11) Airborne transmission of SARS-CoV-2 can occur during medical procedures that generate aerosols ("aerosol generating procedures").(12) WHO, together with the scientific community, has been actively discussing and evaluating whether SARS-CoV-2 may also spread through aerosols in the absence of aerosol generating procedures, particularly in indoor settings with poor ventilation.

The physics of exhaled air and flow physics have generated hypotheses about possible mechanisms of SARS-CoV-2 transmission through aerosols.(13-16) These theories suggest that 1) a number of respiratory droplets generate microscopic aerosols (<5 µm) by evaporating, and 2) normal breathing and talking results in exhaled aerosols. Thus, a susceptible person could inhale aerosols, and could become infected if the aerosols contain the virus in sufficient quantity to cause infection within the recipient. However, the proportion of exhaled droplet nuclei or of respiratory droplets that evaporate to generate aerosols, and the infectious dose of viable SARS-CoV-2 required to cause infection in another person are not known, but it has been studied for other respiratory viruses.(17)

One experimental study quantified the amount of droplets of various sizes that remain airborne during normal speech. However, the authors acknowledge that this relies on the independent action hypothesis, which has not been validated for humans and SARS-CoV-2.(18) Another recent experimental model found that healthy individuals can produce aerosols through coughing and talking (19), and another model suggested high variability between individuals in terms of particle emission rates during speech, with increased rates correlated with increased amplitude of vocalization.(20) To date, transmission of SARS-CoV-2 by this type of aerosol route has not been demonstrated; much more research is needed given the possible implications of such route of transmission.

Experimental studies have generated aerosols of infectious samples using high-powered jet nebulizers under controlled laboratory conditions. These studies found SARS-CoV-2 virus RNA in air samples within aerosols for up to 3 hours in one study (21) and 16 hours in another, which also found viable replication-competent virus.(22) These findings were from experimentally induced aerosols that do not reflect normal human cough conditions.

Some studies conducted in health care settings where symptomatic COVID-19 patients were cared for, but where aerosol generating procedures were not performed, reported the presence of SARS-CoV-2 RNA in air samples (23-28), while other similar investigations in both health care and non-health care settings found no presence of SARS-CoV-2 RNA; no studies have found viable virus in air samples.(29-36) Within samples where SARS-CoV-2 RNA was found, the quantity of RNA detected was in extremely low numbers in large volumes of air and one study that found SARS-CoV-2 RNA in air samples reported inability to identify viable virus. (25) The detection of RNA using reverse transcription polymerase chain reaction (RT-PCR)-based assays is not necessarily indicative of replication- and infection-competent (viable) virus that could be transmissible and capable of causing infection.(37)

Recent clinical reports of health workers exposed to COVID-19 index cases, not in the presence of aerosol-generating procedures, found no nosocomial transmission when contact and droplet precautions were appropriately used, including the wearing of medical masks as a component of the personal protective equipment (PPE). (38, 39) These observations suggest that aerosol transmission did not occur in this context. Further studies are needed to determine whether it is possible to detect viable SARS-CoV-2 in air samples from settings where no procedures that generate aerosols are performed and what role aerosols might play in transmission.

Outside of medical facilities, some outbreak reports related to indoor crowded spaces (40) have suggested the possibility of aerosol transmission, combined with droplet transmission, for example, during choir practice (7), in restaurants (41) or in fitness classes.(42) In these events, short-range aerosol transmission, particularly in specific indoor locations, such as crowded and inadequately ventilated spaces over a prolonged period of time with infected persons cannot be ruled out. However, the detailed investigations of these clusters suggest that droplet and fomite transmission could also explain human-to-human transmission within these clusters. Further, the close contact environments of these clusters may have facilitated transmission from a small number of cases to many other people (e.g., superspreading event), especially if hand hygiene was not performed and masks were not used when physical distancing was not maintained.(43)

Fomite transmission

Respiratory secretions or droplets expelled by infected individuals can contaminate surfaces and objects, creating fomites (contaminated surfaces). Viable SARS-CoV-2 virus and/or RNA detected by RT-PCR can be found on those surfaces for periods ranging from hours to days, depending on the ambient environment (including temperature and humidity) and the type of surface, in particular at high concentration in health care facilities where COVID-19 patients were being treated.(21, 23, 24, 26, 28, 31-33, 36, 44, 45) Therefore, transmission may also occur indirectly through touching surfaces in the immediate environment or objects contaminated with virus from an infected person (e.g. stethoscope or thermometer), followed by touching the mouth, nose, or eyes.

Despite consistent evidence as to SARS-CoV-2 contamination of surfaces and the survival of the virus on certain surfaces, there are no specific reports which have directly demonstrated fomite transmission. People who come into contact with potentially infectious surfaces often also have close contact with the infectious person, making the distinction between respiratory droplet and fomite transmission difficult to discern. However, fomite transmission is considered a likely mode of transmission for SARS-CoV-2, given consistent findings about environmental contamination in the vicinity of infected cases and the fact that other coronaviruses and respiratory viruses can transmit this way.

Other modes of transmission

SARS-CoV-2 RNA has also been detected in other biological samples, including the urine and feces of some patients.(46-50) One study found viable SARS-CoV-2 in the urine of one patient.(51) Three studies have cultured SARS-CoV-2 from stool specimens. (48, 52, 53) To date, however, there have been no published reports of transmission of SARS-CoV-2 through feces or urine.

Some studies have reported detection of SARS-CoV-2 RNA, in either plasma or serum, and the virus can replicate in blood cells. However, the role of bloodborne transmission remains uncertain; and low viral titers in plasma and serum suggest that the risk of transmission through this route may be low.(48, 54) Currently, there is no evidence for intrauterine transmission of SARS-CoV-2 from infected pregnant women to their fetuses, although data remain limited. WHO has recently published a scientific brief on breastfeeding and COVID-19.(55) This brief explains that viral RNA fragments have been found by RT-PCR testing in a few breast milk samples of mothers infected with SARS-CoV-2, but studies investigating whether the virus could be isolated, have found no viable virus. Transmission of SARS-CoV-2 from mother to child would necessitate replicative and infectious virus in breast milk being able to reach target sites in the infant and also to overcome infant defense systems. WHO recommends that mothers with suspected or confirmed COVID-19 should be encouraged to initiate or continue to breastfeed.(55)

Evidence to date shows that SARS-CoV-2 is most closely related to known betacoronaviruses in bats; the role of an intermediate host in facilitating transmission in the earliest known human cases remains unclear.(56, 57) In addition to investigations on the possible intermediate host(s) of SARS-CoV-2, there are also a number of studies underway to better understand susceptibility of SARS-CoV-2 in different animal species. Current evidence suggests that humans infected with SARS-CoV-2 can infect other mammals, including dogs(58), cats(59), and farmed mink.(60) However, it remains unclear if these infected mammals pose a significant risk for transmission to humans.

When do people infected with SARS-CoV-2 infect others?

Knowing when an infected person can spread SARS-CoV-2 is just as important as how the virus spreads (described above). WHO has recently published a scientific brief outlining what is known about when a person may be able to spread, based on the severity of their illness.(61)

In brief, evidence suggests that SARS-CoV-2 RNA can be detected in people 1-3 days before their symptom onset, with the highest viral loads, as measured by RT-PCR, observed around the day of symptom onset, followed by a gradual decline over time.(47, 62-65) The duration of RT-PCR positivity generally appears to be 1-2 weeks for asymptomatic persons, and up to 3 weeks or more for patients with mild to moderate disease.(62, 65-68) In patients with severe COVID-19 disease, it can be much longer.(47)

Detection of viral RNA does not necessarily mean that a person is infectious and able to transmit the virus to another person. Studies using viral culture of patient samples to assess the presence of infectious SARS-CoV-2 are currently limited. (61) Briefly, viable virus has been isolated from an asymptomatic case,(69) from patients with mild to moderate disease up to 8-9 days after symptom onset, and for longer from severely ill patients.(61) Full details about the duration of viral shedding can be found in the WHO guidance document on "Criteria for releasing COVID-19 patients from isolation". (61) Additional studies are needed to determine the duration of viable virus shedding among infected patients.

SARS-CoV-2 infected persons who have symptoms can infect others primarily through droplets and close contact

SARS-CoV-2 transmission appears to mainly be spread via droplets and close contact with infected symptomatic cases. In an analysis of 75,465 COVID-19 cases in China, 78-85% of clusters occurred within household settings, suggesting that transmission occurs during close and prolonged contact.(6) A study of the first patients in the Republic of Korea showed that 9 of 13 secondary cases occurred among household contacts.(70) Outside of the household setting, those who had close physical contact, shared meals, or were in enclosed spaces for approximately one hour or more with symptomatic cases, such as in places of worship, gyms, or the workplace, were also at increased risk of infection.(7, 42, 71, 72) Other reports have supported this with similar findings of secondary transmission within families in other countries.(73, 74)

SARS-CoV-2 infected persons without symptoms can also infect others

Early data from China suggested that people without symptoms could infect others.(6) To better understand the role of transmission from infected people without symptoms, it is important to distinguish between transmission from people who are infected who never develop symptoms(75) (asymptomatic transmission) and transmission from people who are infected but have not developed symptoms yet (pre-symptomatic transmission). This distinction is important when developing public health strategies to control transmission.

The extent of truly asymptomatic infection in the community remains unknown. The proportion of people whose infection is asymptomatic likely varies with age due to the increasing prevalence of underlying conditions in older age groups (and thus increasing risk of developing severe disease with increasing age), and studies that show that children are less likely to show clinical symptoms compared to adults.(76) Early studies from the United States (77) and China (78) reported that many cases were asymptomatic, based on the lack of symptoms at the time of testing; however, 75-100% of these people later developed symptoms. A recent systematic review estimated that the proportion of truly asymptomatic cases ranges from 6% to 41%, with a pooled estimate of 16% (12%–20%).(79) However, all studies included in this systematic review have important limitations.(79) For example, some studies did not clearly describe how they followed up with persons who were asymptomatic at the time of testing to ascertain if they ever developed symptoms, and others defined "asymptomatic" very narrowly as persons who never developed fever or respiratory symptoms, rather than as those who did not develop any symptoms at all.(76, 80) A recent study from China that clearly and appropriately defined asymptomatic infections suggests that the proportion of infected people who never developed symptoms was 23%.(81)

Multiple studies have shown that people infect others before they themselves became ill, (10, 42, 69, 82, 83) which is supported by available viral shedding data (see above). One study of transmission in Singapore reported that 6.4% of secondary cases resulted from pre-symptomatic transmission.(73) One modelling study, that inferred the date of transmission based on the estimated serial interval and incubation period, estimated that up to 44% (25-69%) of transmission may have occurred just before symptoms appeared.(62) It remains unclear why the magnitude of estimates from modelling studies differs from available empirical data.

Transmission from infected people without symptoms is difficult to study. However, information can be gathered from detailed contact tracing efforts, as well as epidemiologic investigations among cases and contacts. Information from contact tracing efforts reported to WHO by Member States, available transmission studies and a recent pre-print systematic reviews suggests that individuals without symptoms are less likely to transmit the virus than those who develop symptoms.(10, 81, 84, 85) Four individual studies from Brunei, Guangzhou China, Taiwan China and the Republic of Korea found that between 0% and 2.2% of people with asymptomatic infection infected anyone else, compared to 0.8%-15.4% of people with symptoms.(10, 72, 86, 87)

Remaining questions related to transmission

Many unanswered questions about transmission of SARS-CoV-2 remain, and research seeking to answer those questions is ongoing and is encouraged. Current evidence suggests that SARS-CoV-2 is primarily transmitted between people via respiratory droplets and contact routes – although aerosolization in medical settings where aerosol generating procedures are used is also another possible mode of transmission - and that transmission of COVID-19 is occurring from people who are pre-symptomatic or symptomatic to others in close contact (direct physical or face-to-face contact with a probable or confirmed case within one meter and for prolonged periods of time), when not wearing appropriate PPE. Transmission can also occur from people who are infected and remain asymptomatic, but the extent to which this occurs is not fully understood and requires further research as an urgent priority. The role and extent of airborne transmission outside of health care facilities, and in particular in close settings with poor ventilation, also requires further study.

As research continues, we expect to gain a better understanding about the relative importance of different transmission routes, including through droplets, physical contact and fomites; the role of airborne transmission in the absence of aerosol generating procedures; the dose of virus required for transmission to occur, the characteristics of people and situations that facilitate superspreading events such as those observed in various closed settings, the proportion of infected people who remain asymptomatic throughout the course of their infection; the proportion of truly asymptomatic persons who transmit the virus to others; the specific factors that drive asymptomatic and pre-symptomatic transmission; and the proportion of all infections that are transmitted from asymptomatic and pre-symptomatic individuals.

Implications for preventing transmission

Understanding how, when and in which settings infected people transmit the virus is important for developing and implementing control measures to break chains of transmission. While there is a great deal of scientific studies becoming available, all studies that investigate transmission should be interpreted bearing in mind the context and settings in which they took place, including the infection prevention interventions in place, the rigor of the methods used in the investigation and the limitations and biases of the study designs.

It is clear from available evidence and experience, that limiting close contact between infected people and others is central to breaking chains of transmission of the virus causing COVID-19. The prevention of transmission is best achieved by identifying suspect cases as quickly as possible, testing, and isolating infectious cases. (88, 89) In addition, it is critical to identify all close contacts of infected people (88) so that they can be quarantined (90) to limit onward spread and break chains of transmission. By quarantining close contacts, potential secondary cases will already be separated from others before they develop symptoms or they start shedding virus if they are infected, thus preventing the opportunity for further onward spread. The incubation period of COVID-19, which is the time between exposure to the virus and symptom onset, is on average 5-6 days, but can be as long as 14 days. (82, 91) Thus, quarantine should be in place for 14 days from the last exposure to a confirmed case. If it is not possible for a contact to quarantine in a separate living space, self-quarantine for 14 days at home is required; those in self-quarantine may require support during the use of physical distancing measures to prevent the spread of the virus.

Given that infected people without symptoms can transmit the virus, it is also prudent to encourage the use of fabric face masks in public places where there is community transmission[1] and where other prevention measures, such as physical distancing, are not possible.(12) Fabric masks, if made and worn properly, can serve as a barrier to droplets expelled from the wearer into the air and environment.(12) However, masks must be used as part of a comprehensive package of preventive measures, which includes frequent hand hygiene, physical distancing when possible, respiratory etiquette, environmental cleaning and disinfection. Recommended precautions also include avoiding indoor crowded gatherings as much as possible, in particular when physical distancing is not feasible, and ensuring good environmental ventilation in any closed setting. (92, 93)

Within health care facilities, including long term care facilities, based on the evidence and the advice by the COVID-19 IPC GDG, WHO continues to recommend droplet and contact precautions when caring for COVID-19 patients and airborne precautions when and where aerosol generating procedures are performed. WHO also recommends standard or transmission-based precautions for other patients using an approach guided by risk assessment.(94) These recommendations are consistent with other national and

[1]Defined by WHO as "experiencing larger outbreaks of local transmission defined through an assessment of factors including, but not limited to: large numbers of cases not linkable to transmission chains; large numbers of cases from sentinel surveillance; and/or multiple unrelated clusters in several areas of the country/territory/area" (https://www.who.int/publications-detail/global-surveillance-for-covid-19-caused-by-human-infection-with-covid-19-virus-interim-guidance)

international guidelines, including those developed by the European Society of Intensive Care Medicine and Society of Critical Care Medicine (95) and by the Infectious Diseases Society of America. (96)

Furthermore, in areas with COVID-19 community transmission, WHO advises that health workers and caregivers working in clinical areas should continuously wear a medical mask during all routine activities throughout the entire shift.(12) In settings where aerosol-generating procedures are performed, they should wear an N95, FFP2 or FFP3 respirator. Other countries and organizations, including the United States Centers for Diseases Control and Prevention (97) and the European Centre for Disease Prevention and Control (98) recommend airborne precautions for any situation involving the care of COVID-19 patients. However, they also consider the use of medical masks as an acceptable option in case of shortages of respirators.

WHO guidance also emphasizes the importance of administrative and engineering controls in health care settings, as well as rational and appropriate use of all PPE (99) and training for staff on these recommendations (IPC for Novel Coronavirus [COVID-19] Course. Geneva; World Health Organization 2020, available at (https://openwho.org/courses/COVID-19-IPC-EN). WHO has also provided guidance on safe workplaces. (92)

Key points of the brief

Main findings

- Understanding how, when and in what types of settings SARS-CoV-2 spreads between people is critical to develop effective public health and infection prevention measures to break chains of transmission.
- Current evidence suggests that transmission of SARS-CoV-2 occurs primarily between people through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings.
- Airborne transmission of the virus can occur in health care settings where specific medical procedures, called aerosol generating procedures, generate very small droplets called aerosols. Some outbreak reports related to indoor crowded spaces have suggested the possibility of aerosol transmission, combined with droplet transmission, for example, during choir practice, in restaurants or in fitness classes.
- Respiratory droplets from infected individuals can also land on objects, creating fomites (contaminated surfaces). As environmental contamination has been documented by many reports, it is likely that people can also be infected by touching these surfaces and touching their eyes, nose or mouth before cleaning their hands.
- Based on what we currently know, transmission of COVID-19 is primarily occurring from people when they have symptoms, and can also occur just before they develop symptoms, when they are in close proximity to others for prolonged periods of time. While someone who never develops symptoms can also pass the virus to others, it is still not clear to what extent this occurs and more research is needed in this area.
- Urgent high-quality research is needed to elucidate the relative importance of different transmission routes; the role of airborne transmission in the absence of aerosol generating procedures; the dose of virus required for transmission to occur; the settings and risk factors for superspreading events; and the extent of asymptomatic and pre-symptomatic transmission.

How to prevent transmission

The overarching aim of the Strategic Preparedness and Response Plan for COVID-19(1) is to control COVID-19 by suppressing transmission of the virus and preventing associated illness and death. To the best of our understanding, the virus is primarily spread through contact and respiratory droplets. Under some circumstances airborne transmission may occur (such as when aerosol generating procedures are conducted in health care settings or potentially, in indoor crowded poorly ventilated settings elsewhere). More studies are urgently needed to investigate such instances and assess their actual significance for transmission of COVID-19.

To prevent transmission, WHO recommends a comprehensive set of measures including:

- Identify suspect cases as quickly as possible, test, and isolate all cases (infected people) in appropriate facilities;
- Identify and quarantine all close contacts of infected people and test those who develop symptoms so that they can be isolated if they are infected and require care;
- Use fabric masks in specific situations, for example, in public places where there is community transmission and where other prevention measures, such as physical distancing, are not possible;
- Use of contact and droplet precautions by health workers caring for suspected and confirmed COVID-19 patients, and use of airborne precautions when aerosol generating procedures are performed;
- Continuous use of a medical mask by health workers and caregivers working in all clinical areas, during all routine activities throughout the entire shift;
- At all times, practice frequent hand hygiene, physical distancing from others when possible, and respiratory etiquette; avoid crowded places, close-contact settings and confined and enclosed spaces with poor ventilation; wear fabric masks when in closed, overcrowded spaces to protect others; and ensure good environmental ventilation in all closed settings and appropriate environmental cleaning and disinfection.

WHO carefully monitors the emerging evidence about this critical topic and will update this scientific brief as more information becomes available.

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WHO continues to monitor the situation closely for any changes that may affect this scientific brief. Should any factors change, WHO will issue a further update. Otherwise, this scientific brief document will expire 2 years after the date of publication.

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