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Transmission of SARS-CoV-2: A Review

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Abstract

The World Health Organization recognized SARS-CoV-2 as a public health concern and declared it as a pandemic on March 11, 2020. Over 12 million people have been affected across several countries since it was first recognized. SARS-CoV-2 is thought to commonly spread through respiratory droplets formed while talking, coughing, and sneezing of an infected patient. Broadly, two modes of transmission of COVID-19 exist direct and indirect. The direct mode includes transmission via aerosols formed through surgical and dental procedures and/or in the form of respiratory droplet nuclei; other body fluids and secretions such as feces, saliva, urine, semen, and tears; mother-to-child. Indirect transmission may occur through fomites or surfaces present within the immediate environment of an infected patient and objects used by the infected person. As many of these modes may be underestimated, it is necessary to emphasize and illustrate them. 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.The aim of this paper is to briefly review how SARS-CoV-2 transmit via various modes and propose measures to reduce the risk of spread within the population.

Key words: Aerosols, COVID-19, Droplets, SARS-CoV-2, Transmission, Populations,

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of coronavirus disease 2019 (COVID-19), has spread worldwide in a few months. This article presents a comprehensive review of the confirmation on transmission of this virus. Although several experimental studies have cultured live virus from aerosols and surfaces hours after inoculation. Strong evidence from case and cluster reports suggests that respiratory spread is dominant, with proximity and ventilation being key determinants of transmission threat. In the few cases where direct contact or fomite transmission is presumed, respiratory transmission has not been completely omitted. The virus has varied transmission dynamics: Most persons do not transmit virus, whereas some cause secondary cases in transmission clusters called ”superspreading events.” Evidence-based practices should incorporate the accumulating knowledge about transmission of SARS-CoV-2 to help

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instruct the public and slow the spread of this virus.

This scientific review presents the consolidation of reviews of publications in peer-reviewed journals undertaken by WHO and partners. 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 review narrates possible methods 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 ranges from mild disease to severe disease and death, and some people infected with the virus never develop symptoms.

i) Contact and droplet transmission

Transmission of SARS-CoV-2 can occur through direct, indirect, or close contact with infected people via infected secretions such as saliva and respiratory secretions or their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings (Liu et al.,2020; Chan et al.,2020; Huang et al.,2020; Burke et al.,2020). Respiratory droplets are >5-10 μm in diameter whereas droplets $\leq$5μm in diameter are referred to as droplet nuclei or aerosols (Ghinai et al.,2020). 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 (Pung et al.,2020). 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.

ii) Airborne transmission

Airborne transmission is defined as the spread of an infectious agent caused by the distribution of droplet nuclei (aerosols) that remain infectious when present in air over long distances and time. Airborne transmission of SARS-CoV-2 can occur during medical procedures that generate aerosols (”aerosol generating procedures”). WHO, together with the scientific community, has been actively evaluating whether SARS-CoV-2 may also spread via 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

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(Mittal etal.,2020; Bourouiba et al.,2020). These theories suggest a number of respiratory droplets generate microscopic aerosols (<5 μm) by evaporating, and 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 (Gralton et al., 2013).

Stadnytskyi et al.,2020 observed the amount of droplets of various sizes that remain airborne during normal speech in his experimental study. However, the authors acknowledge that this has not been validated for humans and SARS-CoV-2. Somsen et al.,2020 found that healthy individuals can produce aerosols via coughing and talking , and another model recommended high variability between individuals in terms of particle emission rates during speech, with increased rates correlated with increased amplitude of vocalization (Asadi et al.,2020). To date, spread of SARS-CoV-2 by this type of aerosol route has not been demonstrated. Experimental studies conducted by Van et al .,2020 and Fears et al.,2020 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 (Van et al ., 2020) and 16 hours in another, which also found viable replication-competent virus (Fears et al.,2020). These findings were from experimentally induced aerosols that do not reflect normal human cough conditions.

Chia ,2020; Guo etal.,2020 and Liu et al.,2020 conducted studies 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. Within samples where SARS-CoV-2 RNA was found, the quantity of RNA detected was in extremely less numbers in large volumes of air and one study that found SARS-CoV-2 RNA in air samples reported inability to identify viable virus (Santarpia et al.,2020). The detection of RNA using reverse transcription polymerase chain reaction (RT-PCR)-based assays is not necessarily indicative of replication- and infection-competent virus that could be transmissible and capable of causing infection (Bullard et al.,2020).

Recent clinical reports of health workers exposed to COVID-19 cases, 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) (Durante et al.,2020; Wong et al.,2020). 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.

Some outbreak reports related to indoor crowded spaces (Leclerc et al.,2020) have

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suggested the possibility of aerosol transmission, combined with droplet transmission, for example, during choir practice (Hamner et al.,2020), in restaurants (Lu et al.,2020) or in fitness centres (Jang et al.,2020). However, the detailed investigations of these clusters where 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 suggest that droplet and fomite transmission could explain human-to-human transmission. 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 (Adam et al.,2020).

iii) Fomite transmission

Respiratory secretions or droplets expelled by infected individuals can contaminate surfaces and objects, creating fomites (contaminated surfaces) (Van et al.,2020; Guo et al.,2020). Viable SARS-CoV-2 virus or RNA detected by RT-PCR can be found on those surfaces for periods ranging from hours to days, depending on the temperature and humidity and the type of surface (Zhou et al.,2020). Viable SARS-CoV-2 virus or RNA are at high concentration in health care facilities where COVID-19 patients were being treated (Ma et al., 2020; Ong et al.,2020) Hence, transmission may also occur indirectly via 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 (Dohla et al.,2020). 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 (Pastorino et al.,2020; Matson et al.,2020).

iv) Other modes of transmission

Guan et al.,2020; Pan et al.,2020; Wang et al.,2020; Wu et al.,2020 and Zheng et al.,2020 detected SARS-CoV-2 RNA in other biological samples, including the urine and feces of some patients. Sun et al., 2020 noticed viable SARS-CoV-2 in the urine of one patient. Xiao et al.,2020 and Zhang et al.,2020 have cultured SARS-CoV-2 from stool specimens. To date, however, there have been no published reports of transmission of SARS-CoV-2 through feces or urine.

Chang et al.,2020 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 blood borne transmission remains uncertain; and low viral titers in plasma and serum suggest that the risk of transmission through this route may be low. At present, 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. 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-

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CoV-2. Transmission of SARS-CoV-2 from mother to child would necessitate 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 breast feed.

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 (Andersen et al.,2020; Zhou et al.,2020). Current evidence suggests that humans infected with SARS-CoV-2 can infect other mammals, including dogs, cats, and farmed mink. However, it remains unclear if these infected mammals pose a significant risk for transmission to humans (Sit et al.,2020; Newman., 2020; Oreshkova et al., 2020).

v) Spread of SARS-CoV-2 from infected person to others

Knowing when an infected person can spread SARS-CoV-2 is just as important as how the virus spreads. 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 (Pan et al.,2020; He et al.,2020; Zou et al.,2020; To et al.,2020 and Wolfel et al.,2020). 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 (Zhou et al.,2020; Xu et al.,2020). In patients with severe COVID-19 disease, it can be much longer (Pan et al.,2020).

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 sparse. Briefly, viable virus has been isolated from an asymptomatic case, from patients with mild to moderate disease up to 8-9 days after symptom onset, and for longer from severely ill patients (Arons et al.,2020). Additional studies are needed to determine the duration of viable virus shedding among infected patients.

vi) Transmission of SARS-CoV-2 via droplets and close contact

SARS-CoV-2 spreads via droplets and close contact with infected symptomatic cases. In an analysis of 76,005 COVID-19 cases in China, 80% of clusters occurred within household settings, suggesting that transmission occurs during close and prolonged contact. A study of the first patients in the Republic of Korea showed that 9 of 13 secondary cases occurred among household contacts (Park et al.,2020). 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 (James et al.,2020). Other reports have supported this with similar findings of secondary

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transmission within families in other countries (Wei et al.,2020).

vii) Transmission of SARS-CoV-2 from SARS-CoV-2 infected persons without symptoms

Preliminary data from China recommended that people without symptoms could infect others. 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 (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 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 (Davies et al.,2020). Kimball et al.,2020 and Wang et al., 2020 informed 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. Multiple studies have shown that people infect others before they themselves became ill (Luo et al.,2020; Jang et al.,2020; Arons et al.,2020).

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. Recent systematic reviews suggests that individuals without symptoms are less likely to transmit the virus than those who develop symptoms (Wang et al.,2020; Luo et al.,2020).

Suggestions for preventing transmission

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 (Lauer et al.,2020). In addition, it is critical to identify all close contacts of infected people so that they can be quarantined 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 (Yu et al.,2020). 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

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measures to prevent the spread of the virus.

It is 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 (Mittal et al., 2020) and where other prevention measures, such as physical distancing, are not possible. Fabric masks, if made and worn properly, can serve as a barrier to droplets expelled from the wearer into the air and environment. 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 (Wu et al.,2020). 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.

WHO continues to recommend droplet and contact precautions within health care facilities when caring for COVID-19 patients and airborne precautions when and where aerosol generating procedures are performed (Alhazzani et al.,2020). WHO also recommends standard or transmission-based precautions for other patients using an approach guided by risk assessment. These recommendations are consistent with other national and international guidelines, including those developed by the European Society of Intensive Care Medicine and Society of Critical Care Medicine and by the Infectious Diseases Society of America (Lynch et al.,2020).

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. 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 and the European Centre for Disease Prevention and Control recommend airborne precautions for any situation involving the care of COVID-19 patients.

Conclusions:

The overarching aim of the Strategic Preparedness and Response Plan for COVID-19 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:

- Identifying suspect cases as quickly as possible, test, and isolate all cases 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.

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