How is the SARS-cov-2 virus transmitted?

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SUMMARY

Since December 2019, the recent outbreak of coronavirus disease (COVID-19) has continued to spread drastically around the world. To date, no approved drug or vaccine is available to treat or prevent this new coronavirus (SARS-CoV-2) infection. Unprecedented global effort has been made by researchers to understand the various routes of SARS-CoV-2 virus transmission in order to effectively prevent the contamination. In this review, we discuss the updated literature regarding the different modes of SARS-CoV-2 transmission.

Introduction

On March 11, 2020, the World Health Organization (WHO) classifies the outbreak due to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) as a public health emergency. This epidemic has just taken the proportions of a pandemic (Gorbalenya et al. 2020). The viral pathology, linked to this Corona Virus, is described in China for the first time in December 2019 and is named COVID-19 (Coronavirus Disease 2019) (WHO 2020). The transmission of this virus reported worldwide, is found on all continents. Until today, November 4, 2020, over 43 million cases have tested positive for SARS-cov-2 which has caused the death of over 1 million of these cases (WHO 2020). It is an enveloped linear single-stranded RNA virus of the beta-coronavirus family with a genome of 29,903 nucleotides (NCBI Reference Sequence: NC_045512.2). SARS-CoV-2 uses the same portal of entry into cells as SARS-COV, the ACE2 receptor on epithelial cells (Z. Liu et al. 2020). The Spike protein on the virus envelope has sufficient affinity with ACE2 to allow entry of the virus into the cell (Z. Liu et al. 2020). Inside it, the viral RNA is replicated by a viral polymerase (RNA dependent RNA polymerase). The transcription and translation steps necessary for the formation of proteins are carried out by the cellular machinery.
The virus assembles in the endoplasmic reticulum, then migrates to the plasma membrane in vesicles to bud and infect other cells (Sicari et al. 2020). The main symptoms of COVID-19 are: fever or a feeling of fever (chills, hot-cold), cough, headache, body aches, unusual fatigue, sudden loss of smell (without nasal obstruction), total disappearance of the taste, or diarrhea and in more serious forms: breathing difficulties that may require hospitalization in intensive care or even lead to death (Y.-C. Wu, Chen, et Chan 2020).

There are two main types of diagnostic tests for SARS-CoV-2 infection. Tests for the direct detection of the virus by the polymerase chain reaction technique (PCR) and serological tests (Caruana et al. 2020). The first type is relatively rapid and well mastered by laboratories. It is carried out on a biological sample, most often nasopharyngeal with a small swab introduced deep into the nose. This sample can also be associated with a sample from the lower respiratory tract (sputum, etc.). The sample is then analyzed in the laboratory in order to directly look for the presence of the genetic material (RNA) of the virus and thus confirm the diagnosis of the infection (Cheng et al. 2020). On the other hand, the second type of diagnostic tests, serological tests, are used to look for the presence in the blood of antibodies directed against SARS-CoV-2 (IgM / IgG). These tests can determine if the person has been infected with the virus in the previous weeks (Cheng et al. 2020). These tests do not allow an early diagnosis of the infection since the production of specific antibodies by the immune system takes a certain time, which can vary from a few days to a few weeks.

Several studies have shown the possibility to detect viral RNA in various body fluid samples. Wang et al detected viral SARS-cov-2 RNA in samples from multiple sites of 205 patients with COVID-19 (W. Wang et al. 2020). Indeed, they detected viral RNA in 93% of bronchoalveolar lavage fluid samples, 72% of sputum samples, 63% of nasal swabs, 32% of pharyngeal swabs, 29% of fecal samples, 1% of blood samples and 0% of urine samples (W. Wang et al. 2020). In addition, several studies have evaluated the SARS-CoV-2 persistence in several different surfaces (Table 1). Transmission of the virus through the respiratory and extrarespiratory routes may help explain the rapid spread of the disease. In this review, we discuss the latest literature regarding the potential of various routes of SARS-CoV-2 transmission.

**Respiratory Transmission**

The principal mode of SARS viruses transmission is through respiratory transmission. Indeed, the virus is transmitted with virions suspended in large droplets of saliva from an infected person (> 5 μm) (Fennelly 2020). These droplets are usually formed by coughing, sneezing, singing, breathing and speaking (Anderson et al. 2020). Inhalation of these respiratory droplets can lead to infection when the healthy person is in direct contact with a patient having symptoms or at a distance of less than 1 m (Organization 2020).

Aerosol transmission also appears to be possible via fine aerosols expelled from the patient’s airways, which would remain longer than the droplets. These fine particles can enter the bronchial and alveolar regions after inhalation, which can lead to infection (Vella et al. 2020).

Social distancing helps decrease infection rate. In fact, a study on the contamination rate of train passengers, which included 2,334 index cases and 72,093 close contacts showed that the infection rate decreased with increasing distance and increased with increasing co-travel time (Hu et al. s. d.). In the other hand, good ventilation can decrease the rate of infection, whereas poor ventilation has been implicated in many transmission groups (James 2020; Furuse et al. 2020). Several studies have shown that wearing a mask can decrease the rate of SARS-COV-2
transmission, which supports the dominant role of respiratory spread of this new virus (Chu et al. 2020; Lee et Jeong, s. d.; Chou et al. 2020).

**Fecal–Oral Transmission**

Until today, several studies have analyzed the possibility of fecal-oral transmission of the SARS-COV-2 virus (Table 2). In Wuhan’s early data, gastrointestinal symptoms like diarrhea, abdominal pain, and vomiting were present in 2-10% of patients with COVID-19 (N. Chen et al. 2020; D. Wang et al. 2020). The mechanisms of SARS-cov-2 interaction with the gastrointestinal tract remain to this day unclear and we believe that this new virus uses ACE2 as a viral receptor.

Xiao et al. have shown that SARS-CoV-2 can be found in stool samples even though it is not detectable in the respiratory tract (Xiao et al. 2020). In Zhang et al. study, all subjects had positive RT-PCR results in the stool after 10 days, with no positive throat swabs, clinical symptoms or imaging results (T. Zhang et al. 2020). Holshue et al. detected SARS-CoV-2 RNA in the stool of a patient in the United States (Holshue et al. 2020).

Prolonged viral detection in fecal samples has also been detected in children after recovery from COVID-19 pneumonia (T. Zhang et al. 2020). This result is supplemented by the Wu et al, study which showed that the viral RNA of SARS-COV-2 can be present in stool samples for nearly 5 weeks after the patient's respiratory samples have been tested negative (Y. Wu et al. 2020). Also, Liu J et al, showed that patients had positive RT-PCR results in anal swabs after recovery (J. Liu et al. 2020). Thus, the virus could remain viable in the environment for days, which could lead to fecal-oral transmission. Indeed, Ong et al. supported the possibility of this transmission by demonstrating extensive environmental contamination of a patient with COVID-19 (Ong et al. 2020). Samples of the surface of the toilet bowl, the interior of the bowl and the door handle were taken from the room of a patient whose feces tested positive for SARS-CoV-2 before routine cleaning. Interestingly, all these samples were positive (Ong et al. 2020). After the routine cleaning, other samples were taken in the same way and all of them were negative this time, implying that current contamination measures such as the use of antiseptics containing ethanol and disinfectants containing chlorine or bleach are effective.

**Vertical Transmission**

Although several studies have evaluated the possibility of vertical transmission of SARS-CoV-2 (Yang et Liu 2020). There is still a need for further conclusive evidence. Some studies have suggested that vertical transmission is possible based on the fact that newborns born to mothers with COVID-19 had elevated IgM antibodies after birth (Kimberlin et Stagno 2020; Zeng et al. 2020). Zeng et al. examined 6 cases of newborns born to mothers with COVID-19 and determined that two of them had elevated IgM levels (Zeng et al. 2020). Also, Dong et al, presented a case of a newborn born to a mother with COVID-19 which tested negative for COVID1-9 on nasopharyngeal samples, but was found to have elevated IgM antibodies 2 hours after his birth (Dong et al. 2020).

Zamaniyan et al. reported the case of a pregnant woman with COVID-19 who gave birth to a premature baby at 32 weeks gestation. The newborn baby showed no signs of infection with SARS-CoV-2. However, the COVID-19 test on the amniotic sample was positive. After 24 hours of her cesarean birth, the nasal and throat test for COVID19 were positive while the tests for COVID19 on vaginal secretion and on the blood of the umbilical cord were negative. Since the amniotic fluid and the newborn have tested positive, this may suggest that the newborn was affected intrauterine
by SARS-CoV-2 (Zamaniyan et al. 2020). A retrospective study of nine COVID-19 pregnant mothers who underwent cesarean delivery, six of them tested negative for COVID19 on amniotic fluid, cord blood, neonatal throat swab, and breast milk (H. Chen et al. 2020). Thus, further studies are needed to further elucidate this vertical transmission mode of SARS-cov-2.

**Ocular transmission**

Transmission of the SARS-cov-2 virus through the ocular surface is now considered a possible route of transmission. Indeed, Lu et al reported the case of a healthcare worker who was infected with the SARS-cov-2 virus after visiting a patient while wearing an N95 respirator, but no protective glasses. These health workers developed redness in their eyes, followed by pneumonia (Lu, Liu, et Jia 2020).

Some studies have noted the detection of viral RNA in conjunctival samples, while others have shown limited evidence for its presence. In a study of 17 cases confirmed to have COVID-19, tears were collected and all samples tested negative for the presence of SARS-CoV-2, while nasopharyngeal samples were positive. In a study of 33 patients with COVID-19 and without ocular manifestation, analysis of ocular secretion samples from two patients (6.1%) revealed the presence of viral RNA (Xie et al. 2020). Colavita et al. analyzed samples from the surface of the eye of a patient with COVID19 almost every day during his hospitalization. Viral RNA was detected until day 21 (and day 27) of his hospitalization (Colavita et al. 2020). Deng et al. reported that of 114 patients with COVID-19 of varying severity, none of the conjunctival secretion samples taken was positive for SARS-CoV-2 RNA (Deng et al. 2020).

In order to demonstrate that ocular swabs samples contained infectious virus, Colavita et al successfully confirmed the viral replication of SARS-cov-2 after inoculating an RNA-positive ocular sample into Vero E6 cells. This implies that the eye fluid of patients with COVID19 may contain an infectious virus and serve as a possible source of infection (Colavita et al. 2020).

**Sexual Transmission**

Sexual transmission of SARS-covid-2 remains uncertain and much discussed. Although ACE2 receptors are expressed in the vagina and testes, no active virus was detected in semen or vaginal secretions (Z. Wang et Xu 2020; Jing et al. 2020). However, during sexual intercourse, transmission of the virus can occur through direct contact and through respiratory droplets and saliva. Although Li et al. reported that viral RNA was detected in the semen of 15.8% of COVID-19 patients (Li et al. 2020), several other studies have failed to confirm the presence of SARS-cov-2 RNA by PCR in semen and vaginal secretions of patients with COVID-19 (Pan et al. 2020; Qiu et al. 2020; Song et al. 2020).

**Conclusion**

This study provides a literature review of the current scientific knowledge about the main mechanisms of SARS-CoV-2 transmission. According to the information available to date, SARS-CoV-2 is spread mainly by respiratory droplets generated when an infected patient coughs or sneezes, and through prolonged close personal contact with an infected patient. Thus, hand hygiene and personal protective equipment can reduce contamination and spread of this disease.
Table 1: Persistence of SARS-CoV-2 virus on different environmental surfaces

<table>
<thead>
<tr>
<th>Study</th>
<th>Environmental surfaces</th>
<th>Persistence</th>
<th>Relative humidity (%)</th>
<th>Temp. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(van Doremalen et al. 2020, 1)</td>
<td>Aerosol</td>
<td>3 ha</td>
<td>65</td>
<td>21–23</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Banknote paper</td>
<td>2 d</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(van Doremalen et al. 2020, 1)</td>
<td>Cardboard</td>
<td>1 d</td>
<td>65</td>
<td>21–23</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Cloth</td>
<td>1 d</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(van Doremalen et al. 2020, 1)</td>
<td>Copper</td>
<td>4 h</td>
<td>65</td>
<td>21–23</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>Cotton</td>
<td>1h4h</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>Gloves (chemical)</td>
<td>4 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>Gloves (nitrile)</td>
<td>7 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>N95 mask</td>
<td>14 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>N100 mask</td>
<td>14 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Paper</td>
<td>30 min</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(van Doremalen et al. 2020, 1)</td>
<td>Plastic (polypropylene)</td>
<td>3 d</td>
<td>65</td>
<td>21–23</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Plastic</td>
<td>4 d</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>Plastics from face shield</td>
<td>21 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(van Doremalen et al. 2020, 1)</td>
<td>Stainless steel</td>
<td>3 d</td>
<td>65</td>
<td>21–23</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Stainless steel</td>
<td>4 d</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>Stainless steel</td>
<td>14 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Surgical mask outer layer</td>
<td>7 d</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Surgical mask inner layer</td>
<td>4 d</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Tissue paper</td>
<td>30 min</td>
<td>65</td>
<td>22</td>
</tr>
<tr>
<td>(Kasloff et al. 2020)</td>
<td>Tyvek</td>
<td>14 d</td>
<td>35–40</td>
<td>20</td>
</tr>
<tr>
<td>(Chin et al. 2020)</td>
<td>Wood</td>
<td>1 d</td>
<td>65</td>
<td>22</td>
</tr>
</tbody>
</table>
Table 2: Fecal-oral transmission of SARS-COV-2 virus

<table>
<thead>
<tr>
<th>Study</th>
<th>Geographic location</th>
<th>Relevant specimen type</th>
<th>Number of positive patients/total number tested (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(X.-W. Wang et al. 2005)</td>
<td>Hubei, Shandong, and Beijing, China</td>
<td>Fecal samples</td>
<td>44/153 (29)</td>
</tr>
<tr>
<td>(J. Zhang, Wang, et Xue 2020)</td>
<td>Beijing, China</td>
<td>Fecal samples</td>
<td>5/14 (36)</td>
</tr>
<tr>
<td>(W. Zhang et al. 2020)</td>
<td>Wuhan, China</td>
<td>Anal swabs</td>
<td>First day of sampling: 4/16 (25) Fifth day of sampling: 6/16 (38)</td>
</tr>
<tr>
<td>(Jiehao et al. 2020)</td>
<td>Shanghai and Qingdao, China</td>
<td>Fecal samples</td>
<td>Day 3–13 after onset of illness: 5/6 (83) Day 18–30 after onset of illness: 5/5 (100)</td>
</tr>
<tr>
<td>(Xiao et al. 2020)</td>
<td>Zhuhai, China</td>
<td>Fecal samples Biopsy tissue from esophagus, stomach, duodenum, and rectum available for one patient</td>
<td>39/73 (53)</td>
</tr>
<tr>
<td>(Tang et al. 2020)</td>
<td>Zhourshan, China</td>
<td>Fecal samples</td>
<td>1/3 (33)</td>
</tr>
<tr>
<td>(Young et al. 2020)</td>
<td>Singapore</td>
<td>Fecal samples</td>
<td>4/8 (50)</td>
</tr>
<tr>
<td>(Kujawski et al. 2020)</td>
<td>AZ, CA, IL, MA, WA, and WI, United States</td>
<td>Fecal samples</td>
<td>7/10 (70)</td>
</tr>
<tr>
<td>(Ling et al. 2020)</td>
<td>Shanghai, China</td>
<td>Fecal samples</td>
<td>54/66 (82)</td>
</tr>
<tr>
<td>(W. Chen et al. 2020)</td>
<td>Guangzhou, China</td>
<td>Anal swabs</td>
<td>11/28 (39)</td>
</tr>
<tr>
<td>(Chan et al. 2020)</td>
<td>Guangdong, China</td>
<td>Fecal samples</td>
<td>0/7 (0)</td>
</tr>
<tr>
<td>(Kam et al. 2020)</td>
<td>Kallang, Singapore</td>
<td>Fecal samples</td>
<td>1/1</td>
</tr>
</tbody>
</table>

Conflicts of Interest

The authors declare that they have no competing interest.

References


• Kujauskis, Stephanie A., Karen K. Wong, Jennifer P. Collins, Lauren Epstein, Marie E. Killerby, Claire M. Midgley, Glen R.


• Wang, Zhengpin, et Xiaojiang Xu. 2020. « ScRNA-Seq Profiling of Human Testes Reveals the Presence of the ACE2 Receptor, A Target for SARS-CoV-2 Infection in


