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Transmission of COVID-19: a brief review of droplet and aerosol transmission routes

Transmissão da COVID-19: um breve reexame das vias de transmissão por gotículas e aerossóis

Abstract

The rapid advance of the COVID-19 pandemic in the year 2020 has spurred researchers to try to understand quickly the behavior of the virus and the disease, and to propose solutions in order to attempt containing it as soon as possible. One of the core questions to be answered is whether the virus can also be transmitted by aerosols, since the mode of transmission determines the speed and conditions under which the disease can spread through the population. The search for this answer has rekindled a decades-long discussion about the relevance of this transmission route, as well as the different concepts and control and prevention measures currently used to block the transmission of infectious diseases in human healthcare. This essay aims to contribute to this debate and, more specifically, to support programs for the protection of workers and patients in healthcare services regarding COVID-19 and other infectious diseases.

Keywords: infectious diseases; infectious disease transmission; infection control; COVID-19; occupational health.

Resumo

O rápido desenrolar da pandemia de COVID-19 no ano de 2020 estimulou pesquisadores a rapidamente tentar entender o comportamento do vírus e da doença e a propor soluções de modo a tentar contê-la o quanto antes. Uma das questões fundamentais a serem respondidas é se o vírus também pode ser transmitido por aerossóis, posto que a forma de transmissão determina a velocidade e as condições em que a doença consegue se espalhar pela população. A busca por essa resposta reacendeu uma discussão de décadas sobre a relevância dessa via de transmissão, bem como sobre os diferentes conceitos e medidas de controle e prevenção atualmente usados para bloquear a transmissão de doenças infecciosas no âmbito da atenção à saúde humana. Este ensaio tem o objetivo de contribuir para esse debate e, mais especificamente, subsidiar programas para a proteção de trabalhadores e pacientes em serviços de saúde referentes à COVID-19 e a outras doenças infecciosas.

Palavras-chave*: doenças infecciosas; transmissão de doença infecciosa; controle de infecções; COVID-19; saúde do trabalhador.*

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Introduction

Although exposure to airborne microorganisms is a common occurrence in human life[1], most infectious diseases are considered to be transmitted by direct contact or fomites, with airborne or aerosol transmission playing a minor or secondary role, except in a few cases, such as tuberculosis or measles[2,3]. For years, however, medical and scientific communities have been accumulating evidence of the relevance of this transmission route in hospital infection outbreaks, and in the dissemination of different infectious diseases among the population[1,2].

Such research has gained momentum since 2003, with the outbreaks of Severe Acute Respiratory Syndrome (SARS) caused by the coronavirus SARS-CoV, and underwent new impetus in 2009, with the emergence of influenza A, caused by H1N1 influenza virus and, in 2014, with the emergence of Middle East Respiratory Syndrome (MERS), caused by coronavirus MERS-CoV[4,5]. Now, with the pandemic of COVID-19, 241 scientists of different nationalities have subscribed to a publication addressed to the medical community and to national and international institutions to recognize the potential for the spread of this disease by the airborne route, i.e. airborne or aerosol transmission[6]. This caused the World Health Organization (WHO) to partially revise its initial judgment regarding the transmission routes of COVID-19, admitting that airborne transmission could not be ruled out, especially indoors[7].

Identifying the origin of the reluctance to recognize the importance of airborne transmission takes us back in time to 1910, when the paradigm of transmission by miasms, which was very common until then, was replaced by the current paradigm that most respiratory diseases are transmitted directly by droplets at short distances or after contact with contaminated fomite or surfaces[3,8], respectively termed direct droplet transmission and indirect contact transmission[8].

There are other factors that also contribute to minimize airway as a significant route for infectious disease transmission. First, the two most epidemiologically relevant airborne diseases, tuberculosis and measles, have been controlled with reasonable success by vaccination or drug treatment, diminishing the interest in understanding the aerobiology involved[3]. Secondly, it is relatively easy to identify contamination of water, surfaces and fomites, and transmission that originates in droplet formation. Proving air contamination, however, is more difficult because infectious aerosols are usually very dilute, and it is also laborious to collect and culture microorganisms from this material[3]. For health services, there are also significant implications in terms of increased costs for the implementation of specific protection and control measures, and changes in work organization related to the adequate care of infected patients, associated with the recognition of a disease as potentially transmissible by the airborne route[9].

Regardless of the difficulties and costs involved, however, there is now robust evidence that infectious diseases are transmitted by multiple routes, including airborne transmission[2,3,10,11]. Furthermore, since contaminants in fomites and surfaces may come from the air, it should be admitted that air also plays a role in transmission through indirect contact with fomites and surfaces[2]. Therefore, the relatively rigid and almost exclusive classification of infectious diseases transmission by direct contact, indirect contact, droplet contact, and airborne routes should be revisited to allow for a more nuanced approach to multiple transmission routes, i.e., transmission by more than one route simultaneously, without one overriding or excluding the other.

This essay was developed from a narrative review of literature, with emphasis on scientific articles and publications questioning and discussing the airborne transmission of infectious diseases – especially after the emergence of the SARS-CoV virus in 2003 – and national and international recommendations and guidelines on the subject published by the Brazilian Ministry of Health, the National Health Surveillance Agency (Anvisa), the *Fundação Jorge Duprat Figueiredo de Segurança e Medicina do Trabalho* (Fundacentro), the U.S. Centers for Disease Control and Prevention (CDC), and the WHO, particularly the guidelines related to tackling COVID-19. This text aims to synthesize evidence and concepts related to airborne transmission, before and after the onset of the pandemic. It also aims to contribute to the discussion of associated protective measures that could be adopted in several health services for the protection of both workers and patients.

Droplets and aerosols: concepts and characteristics

Aerobiology is the study of the processes involved in the movement of microorganisms in the atmosphere, also covering the transmission of diseases by aerosols[1]. Advances in this science and in knowledge of infectious diseases and forms of exposure, as well as in the field of occupational hygiene, have significantly expanded the understanding of transmission routes and the ability to plan and implement effective controls[12].

By definition, an aerosol is a suspension of particles in a gas, comprising solid particles, liquids, or mixtures that, depending on the combination of their physical characteristics and environmental conditions, remain in the air long enough to be transported by air currents[1,12]. The time they remain suspended varies, but initial studies on aerosol physics from the 1930s showed that this period is at least a week, and it was suggested later that it could be even longer[1]. As for the distance traveled, aerosols can easily be located up to 20 meters from their origin, depending on various environmental factors such as weather conditions, effects of fluid dynamics, and indoor pressure differentials[1].

The term "bioaerosol", in turn, covers all particles of biological origin that are distributed in the atmosphere[13]. A bioaerosol can be of vegetal or animal origin, or it can consist of or contain large quantities of microorganisms, including: bacteria, such as the genera *Legionella* or *Actinomycetes*; fungi, such as the genera *Histoplasma*, *Alternaria*, *Penicillium* and *Aspergillus*; protozoa, such as the genera *Naegleria* and *Acanthamoeba*; and, finally, viruses, such as the influenza virus[13].

Bioaerosols vary greatly in size. Viruses are commonly smaller than 0.2 μm, while bacteria, spores and fungal cells are between 0.25 and 60 μm[13]. Usually, bioaerosol does not consist of just the microorganism alone or a single microorganism, normally containing large amounts of microorganisms. The diameter of various pollen types ranges from 5 to 300 μm[13]. Tiny arthropods such as mites, which are transported through the atmosphere and form the so-called "aeroplankton", can be as large as 1 mm[13]. Large variations in size are also observed in airborne cell fragments or colonies, within a range of nanometers to hundreds of micrometers[13].

Liquid particles up to 100 μm in diameter can remain suspended for long periods under certain conditions of air motion[1], and in meteorology, droplets are liquid particles up to 200 μm in suspension in clouds or that evaporate before reaching the ground[12]. Fog droplets can reach over 20 μm in diameter, although most do not exceed 10 μm[12]. This means that, for meteorology, the droplets that form clouds or fog correspond to aerosols, because they are suspended in the air.

All this evidence from different sciences and fields indicates that there are inconsistencies in the concepts of "respiratory droplets" and "aerosols" used in the health field, and shows that these concepts do not correspond to those used in meteorology, aerobiology, and occupational hygiene[12]. So, one of the first steps to effective control of airborne transmission is to homogenize this mutual understanding.

When breathing, talking, coughing, and sneezing, humans produce droplets between 0.1 and 1,000 μm[14] that are composed of a mixture of solids and liquids. Their size and inertia, influenced by gravity and evaporation, help determine how far they travel from their source[14]. Because of gravity, larger respiratory droplets fall before evaporating, thus contaminating the ground and other surfaces and leading to transmission by indirect contact. Smaller droplets evaporate before falling, and the solids in them constitute the so-called droplet nuclei, which remain in suspension and are carried by air currents for distances greater than two meters[7,10,14], characterizing airborne transmission.

In the health area , the WHO and the CDC have established "droplet transmission" as the spread of an infection or infectious disease involving particles larger than 5 μm, and "airborne transmission" as that which occurs with particles of diameter equal to or less than this value[7,8,14]. Respiratory droplets with a diameter greater than 5 μm correspond to "droplets", while the term "aerosol" applies only to droplet nuclei with a diameter equal to or smaller than that[7].

As proposed by the WHO, therefore, droplet transmission occurs when an infected person releases contaminated respiratory droplets larger than 5 μm that reach the mucous membranes of the mouth, nose, or eyes of another person up to one meter away and start an infection in that person[7]. In other words, when these droplets are thrown in the form of a spray, acting as small projectiles that directly strike the mucous membranes of the exposed person, who then develops an infection[12]. These droplets can also lead to infection of an exposed person after contact with objects or surfaces onto which they have been thrown or projected, characterizing transmission by indirect contact[7].

Aerosol transmission, on the other hand, occurs when an exposed person is infected by inhaling droplet nuclei that are 5 μm or less, and contain viable doses of the infectious agent even after they have been airborne for longer distances and times[7].

Thus, the prevailing view is that the 5 μm diameter of the particle is what differentiates droplets from aerosols and separates droplet transmission from airborne transmission[11]. The CDC, however, reports that particles of 30 μm or more may remain suspended in the air[15]. This understanding also implies, in practice, that the agent transmitted by direct or indirect contact with droplets is not transmitted by aerosols and vice-versa, configuring a false dichotomy between these two routes of transmission.

Thus, this way of differentiating droplets from aerosols and of characterizing the transmission routes ignores the accumulated evidence, contradicts the concepts adopted in other sciences, and has hindered the broader understanding of respiratory disease transmission[8,11-13,16]. In view of the COVID-19 pandemic, several researchers are debating and shedding light on this issue in order to provide a satisfactory response to this challenge.

One of the initiatives was a virtual workshop on the subject – Airborne Transmission of SARS-CoV-2 – organized by the National Academies of Sciences, Engineering, and Medicine in August 2020[16]. The event annals, published in October, proposed a unified terminology to better differentiate between droplets and aerosols, and the transmission routes associated to them[16]. It was also suggested that the term aerosol be used to describe a stable suspension of solid, liquid, or mixed particles up to 100 μm in diameter in air, restricting the term droplet to predominantly liquid particles larger than 100 μm[16]. These and other information have been summarized in **Chart 1**.

Chart 1 Terminology of particles involved in airborne transmission of pathogens

Traditional descriptions[a]			
Terms	*Definition and typical size*		
Aerosol[b]	Particle or droplet nucleus $\leq 5\,\mu$m		
Droplet	Liquid particle[c] $> 5\,\mu$m		
Updated descriptions[d]			
Terms	*Definition and typical size*	*Route of exposure or transmission*	*Behavior in air*
Aerosol	Stable airborne suspension of solid, liquid, or mixed particles $< 100\,\mu$m in diameter	Inhaled into the respiratory system	- May remain in suspension for longer periods. - Concentration is significantly higher near the emitting source. - Concentration decreases as distance from source increases, but can travel farther than about 2 meters. - Accumulates in enclosed spaces.
Droplet	Liquid particle with diameter $> 100\,\mu$m	Direct contact with mucous membranes of eyes, nose and mouth of people who are very close.	- Deposits rapidly on the ground or other surfaces. - It is transported for less than 2 meters, except when propelled, i.e., when ejected with speed during sneezing or coughing.

[a] Based on long-standing misconceptions, not supported by aerosol physics.

[b] The term aerosol is short for "aerosol particle", reflecting its common usage.

[c] By liquid particle is meant a predominantly liquid particle, in which the solid part represents only a tiny fraction of the total.

[d] Prepared according to aerosol physics and data on exposure pathways.

Source: Adapted from National Academies of Sciences, Engineering, and Medicine[16].

Not only do these updated definitions of droplets and aerosols correspond more consistently to those used in other areas to refer to aerosols and bioaerosols[13], they are also more compatible with the characterization and classification developed by occupational hygiene, based on aerosol size, potential penetration capacity, and sites of deposition in different regions of the respiratory tract[12,17]. The "respirable fraction" is composed of aerosols or particulates up to 5 μm in diameter that usually penetrate beyond the terminal bronchioles and deposit in the alveoli; "thoracic fraction" corresponds to aerosols or particulates up to 15 μm in diameter that pass through the larynx and penetrate the trachea and bronchi; and "inhalable fraction" comprises aerosols or particulates with diameters between 100 and 200 μm that enter through the nostrils and mouth and enter the respiratory tract[12,18]. The great variability related to health condition and breathing capacity, breathing patterns (rate and airway), anatomical differences in the airways, and the level of activity at any given time entails significant uncertainties in the doses and deposition sites of these fractions for each individual[18]. Therefore, occupational hygienists have established more conservative sampling criteria in order to overestimate lung exposure, thus providing greater protection to exposed workers[18]. Thus, to compose the respirable fraction, aerosols or particulates of up to 10 μm are collected, with 50% of the sample having up to 4 μm; for the thoracic fraction, material of up to 25 μm is collected, with 50% of the sample having up to 10 μm; and for the inhalable fraction, aerosols or particulates of up to 100 μm are collected[17,18].

Determining the fraction of aerosols involved in transmission is important because infection and disease also depend on the tissue where deposition occurs. For example, in the case of *Mycobacterium tuberculosis*, the agent of tuberculosis, since the target tissue is almost exclusively the alveoli, the respirable fraction is much more relevant than any other fraction[12]. For SARS-CoV-2, probably all the particulate fractions, respirable, thoracic, and inhalable, are important, because its target tissues range from the mucous membranes of the upper respiratory tract to the alveoli[12].

Note that, in all these cases, exposure occurs through the inhalation of particulates suspended in the air, that is, it is characterized as airborne or aerosol transmission. Droplet transmission, on the other hand, would apply only when the respiratory droplets are larger than 100 μm.

These changes affect the recommended protective measures against respiratory disease agents, always aiming to make them more effective and comprehensive, a topic that will be addressed below.

Measures recommended in healthcare services

Traditionally, protective measures in health services are grouped into standard precautions and specific or transmission-based precautions. This is the primary strategy for control and protection against infectious biological agents in health services[15]. They include engineering, administrative and work organization controls, ergonomic measures, vaccination, correct and researched practices for daily routine, and use of personal protection equipment (PPE)[19]. Standard precautions are applicable to the care of all patients, and aim to prevent transmission from blood or other fluids by direct or indirect contact[15,19]. Specific precautions are employed in addition to standard precautions and aim to block transmission routes not covered by them. They are applied to care of patients with suspected infectious disease transmitted by other routes[15].

Specific precautions for the care of patients with suspected communicable respiratory diseases are precautions taken to avoid direct or indirect contact with droplets and inhalation of aerosols[15,20], and should be applied to suspected cases even before they are confirmed. In both cases, patient isolation, rapid identification of the pathology, use of surgical mask by the patient, limited transportation, and restricted visits are required[15,20]. They differ, however, regarding the degree of patient isolation, health professional's individual respiratory protection, and requirements for ventilation of the facility.

Patients in isolation for droplets and infected with the same agent can be admitted to the same room as long as a distance of one meter between beds and their separation with curtains is ensured[15,20]. On the other hand, patients with airborne diseases should be isolated in private rooms, with the doors always closed[15,20].

For droplet precautions, the professional should wear a surgical mask whenever they have contact with the patient, and it should be placed before entering the room; while for aerosol precautions, they should use at least a P2 (PFF2) respirator, equivalent to the N95 mask of the American classification, during the entire care[15,20].

As aerosols can be transported over longer distances, it is necessary to have special engineering controls, such as specific ventilation systems that prevent their dissemination inside a facility. In the case of droplets, the probability of airborne dissemination is small, then such ventilation systems or stricter air quality control are not necessary[15].

Thus, while there is no requirement for ventilation or air control in droplet precautions, aerosol precautions require the patient's room to have negative pressure, six to twelve air changes per hour, and air filtration with high efficiency filters if there is recirculation[15,20]. If the institution does not have rooms with these characteristics, the private room should be kept with its doors closed and the windows open to allow good ventilation[20].

According to the Brazilian Ministry of Health, COVID-19 would be transmitted by droplets and, therefore, the corresponding precautionary measures would apply[21,22]. In its recommendations, it informed that aerosol transmission was still being studied and that, at that time, there was no robust evidence to support it[21,22]. It clarified that airborne transmission of COVID-19 was plausible in medical procedures capable of generating aerosols, and so in these situations droplet precautions should be replaced by aerosol precautions[21,22]. The medical procedures exemplified by the Brazilian Ministry of Health included tracheal intubation, open tracheal suction, tracheostomy, non-invasive mechanical ventilation, disconnecting the patient from the ventilator, cardiopulmonary resuscitation, manual ventilation before intubation, nasotracheal sampling, bronchoscopies, and administration of treatment by nebulization[21,22].

The WHO adopted the same position and published very similar guidelines in July 2020[7]. However, the organization acknowledged that it could not rule out airborne transmission of COVID-19, particularly in crowded and inadequately ventilated indoor spaces[7], reporting that this type of transmission had not been found in healthcare settings until then[7].

But if the conditions are present in these facilities, it is reasonable to assume that aerosol transmission may also occur there.

Following this argumentation, the WHO concluded its recommendations against COVID-19 by suggesting the following additional measures: maintain physical distance from other people whenever possible; avoid crowded places or proximity to other people; avoid enclosed or confined spaces with poor ventilation; and ensure good ventilation of enclosed spaces, in addition to appropriate cleaning and disinfection[7].

The Brazilian Ministry of Health has also emphasized the importance of health services having environments with abundant ventilation and open windows in waiting rooms and isolation areas[21,22].

Thus, it can be observed that both the WHO and the Brazilian Ministry of Health recommended measures related to ventilation and air control in closed spaces, which goes beyond droplet precautions.

Later, in October 2020, the CDC published a scientific report[23] directly addressing the issue of airborne transmission of SARS-CoV-2. In it, there are two key points about airborne transmission applied to COVID-19 that might be extended to other diseases. The most recent update to this report is from May 2021.

The first point is the inclusion of the term "particle" in the description of aerosol and not delimiting airborne transmission to aerosols of specific diameters, but recognizing that it can occur in cases involving contaminated droplets or particles of any size[23].

The second point is the characterization of airborne transmission of COVID-19 as the primary route of transmission[23], and in circumstances other than those related to the aerosol generating procedures described above and similar to the airborne transmission detailed by WHO[7]. These circumstances involve a person producing contaminated aerosols for at least 15 minutes in an enclosed, poorly ventilated space, especially if they are making expiratory effort, such as when shouting, singing, or exercising[23]. This then allows the accumulation of virus in the air in sufficient quantity to infect people more than two meters away from the infected individual or who entered that space shortly after he or she left[23].

The evidence available for COVID-19 so far allows to preliminarily establishing a special airborne transmission, in contrast to that observed in known airborne diseases, that can occur outside of closed, poorly ventilated spaces, even if the susceptible individual entered the environment hours after the infected person had left and without the infected person having made any expiratory effort. It is very difficult to prove airborne transmission of an infectious disease, which is why only those that are very efficient at being transmitted by this route, after inhalation of very small doses of the respective pathogens, are recognized as such[3], as is the case with tuberculosis, measles and chickenpox. Therefore, although the prevention of special airborne transmission does not require the implementation of some engineering controls required by aerosol precautions, extra measures are needed to improve ventilation and prevent crowding in enclosed spaces[23], exactly as recommended by the WHO[7] and provided by the Brazilian Ministry of Health[21,22].

Recommended measures in health services: changes prompted by COVID-19

What the evidence suggests so far, at least preliminarily, is that airborne transmission could be divided into two types: the already known, medium- to long-range, low airborne pathogen concentrations characteristic of diseases such as tuberculosis, measles, and chickenpox; and a special, short- to medium-range (room or room size) airborne transmission in enclosed spaces and with high airborne pathogen concentrations. In the case of COVID-19, the disease is transmitted through both direct contact or droplet transmission and special airborne transmission.

In order to prevent or minimize the transmission of COVID-19 in healthcare settings, it is suggested that, in addition to adopting droplet precautions and other recommendations from the Brazilian Ministry of Health,[21,22] the following additional measures, based on CDC recommendations[24], should also be considered:

a) implement or maintain telemedicine procedures whenever possible;

b) encourage physical distancing of at least 2 meters between people, define open-air areas whenever possible, limit the number of visitors to what is strictly necessary, organize processes to reduce the number of patients in waiting rooms, rearrange these rooms to maintain a distance of 2 meters between people, implement open-air waiting rooms or screening areas, or allow people to wait in their own cars when seeking care;

c) as long as the community transmission continues, all healthcare workers should wear at least a face-fitted surgical mask and eye protection during care of all patients; and, for care of suspected or confirmed cases of COVID-19, PFF2 or N95 respirators together with eye protection, even for procedures that do not generate aerosols;

d) explore options, in consultation with facility engineers, to improve indoor air quality in all shared spaces, including optimizing ventilation systems (airflow direction, filtration, air exchange rates, adequacy and maintenance of facilities), and purchasing portable air filtration equipment in locations where the use of ventilation systems is not possible.

Given that other pathogens, including *Aspergillus* spp, *Bordetella pertussis*, *Clostridium difficile*, SARS-CoV (SARS agent), respiratory syncytial virus, rubella virus, *Histoplasma capsulatum*, influenza A virus, *Legionella pneumophila*, mumps virus, norovirus, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pyogenes*, could also be transmitted by aerosols[2], at least under certain circumstances, so the additional measures mentioned in the previous paragraph could also help in the prevention of diseases caused by these other agents.

Data and evidence on the possibility that different infectious biological agents can be transmitted by aerosols have been accumulating, especially since the first outbreaks involving a coronavirus, as recently as 2003. Since that year, the scientific community has been deepening research on the topic, and alerting health authorities and governments, whose technical recommendations have also been gradually changed in this direction. A demonstration of that can be found in the CDC's 2007 Guideline for Isolation Precautions, which suggest expanding airborne transmission to agents other than tuberculosis and measles, and classifying it as mandatory, preferential, or opportunistic[15]. This change can also be seen in the respiratory protection booklet published by the Brazilian Ministry of Health in 2009, which includes several species of hantavirus, the SARS agent coronavirus, *Bacillus anthracis*, the influenza virus strain H5N1 (avian influenza) in the list of airborne agents in addition to the already known agents of tuberculosis, measles, and chickenpox[20].

Final considerations

A pandemic always brings enormous damage to society. Like every crisis, it also represents an opportunity to review the ideas and practices used for the prevention and control of these diseases, with the potential for immediate and future corrections and advances. Thus, the current pandemic of COVID-19 also represents a stimulus for the reformulation of guidelines and recommendations related to measures for prevention and control of transmission of infectious diseases in healthcare services.

As an introductory essay and the result of a non-exhaustive review of the literature, this text necessarily suffers from limitations as to its scope, even more so in view of the fact that knowledge on this subject is currently being updated and modified very rapidly. We hope this paper has simplified and summarized the information and evidence currently under debate about the concepts of droplets and aerosols, droplet and airborne transmission, and associated precautionary measures, thus contributing to safer and healthier work environments for healthcare workers and patients.

Author contributions

Reinhardt EL conceived the argument, performed the information gathering, and drafted the essay, and takes full responsibility for the work done and the content published.

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