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REVIEW

Transmission routes, preventive measures and control strategies of SARS-CoV-2 in the food factory

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ABSTRACT
SARS-CoV-2 virus represents a health threat in food factories. This infectious virus is transmitted by direct contact and indirectly via airborne route, whereas contamination through inanimate objects/surfaces/equipment is uncertain. To limit the potential spread of the pathogen in the food industry, close working between individuals should be avoided and both personal and respiratory hygiene activities should be enforced. Despite the high infectivity, SARS-CoV-2, being an enveloped virus with a fragile lipid envelop, is sensitive to biocidal products and sanitizers commonly used in the food factory. In the context of the building design, interventions that promote healthy air quality should be adopted, especially in food areas with high-occupancy rates for prolonged times, to help minimize the potential exposure to airborne SARS-CoV-2. Air ventilation and filtration provided by heating, ventilation and air conditioning systems, are effective and easy-to-organize tools to reduce the risk of transmission through the air. In addition to conventional sanitation protocols, aerosolization of hydrogen peroxide, UV-C irradiation or *in-situ* ozone generation are complementary techniques for an effective virucidal treatment of the air.

KEYWORDS
SARS-CoV-2; sanitation; ventilation; UV-C light; ozone; hydrogen peroxide aerosolization

Introduction

The Coronavirus Study Group of the International Committee on Taxonomy of Viruses termed the causative agent of the pandemic outbreak emerging in China in December 2019 as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Gorbalenya et al. 2020). The corresponding disease was named coronavirus disease-19 (COVID-19) (Gorbalenya et al. 2020). Phylogenetically and taxonomically, this virus is a sister to SARS-CoVs, being classified into the family *Coronaviridae*, genus *Betacoronavirus* and subgenus *Sarbecovirus*. Chan et al. (2020) demonstrated that SARS-CoV-2 is a distinct lineage closely related to bat SARS-like CoVs in the subgenus *Sarbecovirus*. Based on the whole-sequence alignment, SARS-CoV-2 shares 96% and 82% identity with bat CoV RaTG13 and SARS-CoV, respectively, thus confirming the zoonotic origin. SARS-CoVs are able to cross the species barrier, causing the infection in a new target species and a variety of diseases in man and animals (Helmy et al. 2020). Since the ´60s, six human CoVs (HCoVs) have been documented and recognized (Table 1). In detail, CoVs 229E, NL63, OC43 and HKU1 cause mild illness similar to the common cold and gastrointestinal tract infection (Helmy et al. 2020). Differently, zoonotic infections by SARS-CoV in 2003 and Middle East Respiratory Syndrome (MERS)-CoV in 2012 raised significant public health concerns, causing high pathogenicity and mortality in humans (Wu et al. 2020). Bats are currently considered the natural reservoir for all HCoVs. SARS-CoV was transmitted to palm civets as intermediate host and then to humans, whereas MERS-CoV to dromedary camels and subsequently to humans. The intermediate host that SARS-CoV-2 originated from is still unclear. This new-emerging HCoV has been causing severe respiratory illness and mortality. As of 2nd of August 2020, COVID-19 caused more than 17.6 million clinically-diagnozed illnesses and 680,894 deaths across the globe (WHO 2020a).

Human CoVs are enveloped viruses with a single-strand RNA genome and a mean diameter in the range 80-220 nm. Typically, CoVs, within the lipid bilayer of the envelope, have four structural proteins along with a variety of minor components, including accessory proteins, which are associated to membrane deformation and are required at various stage of the virus replication cycle (Alsaadi and Jones 2019).

This review is intended to investigate the transmission routes of SARS-CoV-2 in food factories, highlighting the potential spreading of the virus as well as the counteractive actions based on personal hygiene practices and environmental sanitation procedures. The focus is also addressed to evaluate complementary techniques to counteract the airborne route transmission of the virus.

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Table 1. Classification of human coronaviruses according to the International Committee of Taxonomy of viruses (modified from Helmy et al. 2020).

Genus	Species	Abbreviation	Zoonotic	Reservoir	Year of identification
Alphacoronavirus	Human coronavirus 229E	HCoV-229E	No	Humans	1966
	Human coronavirus NL63	HCoV-NL63	No	Humans	2004
Betacoronavirus	Betacoronavirus-1	HCoV-OC43	No	Humans	1967
	Human coronavirus HKU1	HCoV-HKU1	No	Humans	2005
	Middle East respiratory syndrome-related coronavirus	MERS-CoV	Yes	Bats, camels and humans	2012
	Severe acute respiratory syndrome-related coronavirus	SARS-CoV	Yes	Bats, palm civets and humans	2003
	Severe acute respiratory syndrome-related coronavirus	SARS-CoV-2	Yes	Bats, ?, humans	2019

Routes of transmission of SARS-CoV-2

The transmission mechanisms of respiratory diseases are a subject for debate and are affected by several parameters, namely physical (respiratory particles and droplet generation), virological (viral load, survival), behavioral (person-to-person distance, handshaking, surface contact) and environmental (temperature, humidity, ventilation) (Dietz et al. 2020; Tang et al. 2006). Understanding the complex multi-route transmission mechanisms is of major relevance to implement proper intervention methods. Widely recognized transmission routes of SARS-CoV-2 include direct contact (e.g., hugging, touching and shaking hands), contact with close-released droplets and the airborne or aerosol route (Morawska et al. 2020).

Transmission by droplets

SARS-CoV-2 effectively spreads between humans via respiratory close-contact large droplets (Rothe et al. 2020). The transmission route by droplets consists in the close exposure of a susceptible person to the virus contained in the respiratory secretions of an infector (coughs, sneezes or talks). The exhaled particles of saliva dissipate in the air over time and distance and may be directly inhaled or come in contact with mucous membranes (conjunctivae, mouth, nasal, throat or pharynx mucosa). Xie et al. (2007) showed that the size of particles that would fall to the ground within 2 m is 60-100 µm and these can be carried more than 6 m away by sneezing. The dimensional characterization of excreted particles has a sanitary meaning, because droplets approximately larger than 100 µm cannot be directly inhaled, but they may land in the head airways. Smaller particles penetrate deeper in the lower respiratory airways, likely having a different dose-response pattern (Gao et al. 2021). To the best of our knowledge, to date, there are no studies confirming the transmission of COVID-19 disease via this route.

Airborne or aerosol route (long range and small size droplets route)

In the health care setting, WHO defined airborne transmission as the spread of an infectious agent caused by the dissemination of "droplet nuclei" (i.e., the residues of droplets after desiccation with a size smaller than 5 μm). The droplet nuclei are rapidly formed (for instance, a droplet with a 10 µm diameter evaporates in 0.2 s) (Rehva 2020). Relative humidity (RH) affects the evaporation process of droplets, in particular the air with a higher level of RH has a lower potential in absorbing the water vapor. By using a theoretical model, Liu et al. (2019) calculated the droplet suspension time as a function of RH. In particular, the authors observed that at levels of 20% and 50% RH a 10 µm droplet desiccated in 0.1 and 0.7 s, respectively. Droplet nuclei remain infectious when suspended in air over long distances and time (Siegel et al. 2019). Obviously, it is important whether pathogens are in these plumes and whether their size is consistent with transmission (Fennelly 2020). Several research studies proved that airborne route was involved in the spread of SARS-CoV and MERS-CoV (Adhikari et al. 2019; Kulkarni et al. 2016; Wang, Feng, et al. 2020). Whether SARS-CoV-2 spreads through small particles remaining in the air over time and distance is controversial, being related to the virus survivability. To the best of our knowledge, there are no published reports of cough aerosol from patients with COVID-19 responsible for the transmission of the disease. Biological factors, such as the size of the emitted inoculum, the virus ability to survive desiccation and other stress conditions of aerosolisation and airborne transport, as well as air movements, temperature and humidity, and host defenses explain the variability of transmission among respiratory pathogens. van Doremalen et al. (2020) reported that SARS-CoV-2 grown in tissue culture after aerosolization (to particles with size $<$ 5 µm) showed only a slight reduction in viability after 3 h (i.e., from 3.5 $\log_{10}$ to 2.7 $\log_{10}$ units of 50% tissue culture infectious dose, $TCID_{50}$, per liter of air). However, the experimentally induced aerosol-generating procedure did not reflect the normal human cough conditions. A field report revealed the occurrence in the air of a hospital in Wuhan of SARS-CoV-2 RNA with 0.02 RNA copies L^{-1} in a toilet area and 0.02–0.04 copies L^{-1} in a room used to remove personal protective equipment, although the infectivity of the virus was not known (Liu et al. 2020). More than half the viral RNA in these samples was associated with aerosols $<$ 2.5 μm. In addition, the authors measured through passive aerosol samplers, located approximately 2 m and 3 m from the patients, deposition rates of 31 and 113 RNA copies m^{-2} h^{-1}, respectively. Despite these data suggest that SARS-CoV-2 in real-scenarios may be non-negligible sources of airborne SARS-CoV-2, the infectivity of the virus was not investigated. In another study, Wang, Feng, et al. (2020), in the isolation room of a COVID-19 positive patient, observed that SARS-CoV-2 RNA was undetectable in air samples near the patient, whereas surface samples collected in the sewage pool of the hospital isolation area resulted positive. The authors concluded that the adopted ventilation conditions ($>$ 12 air exchanges per hour) allowed to rapidly diluting the exhaled air inside the room, thus making airborne transmission of SARS-CoV-2 of low relevance.

Overall, the clear distinction between airborne (long-range and small size, i.e. > 1 m and < 5 µm, respectively) and droplets (short-range and large size, i.e. < 1 m and > 5 µm) routes operated by international organizations is somewhat ambiguous. Indeed, it is known that large droplets (> 5 µm) may easily remain suspended and dispersed over 1 m as a function of the natural or mechanical ventilation in the indoor environment (Morawska 2006). For this reason, infection routes cannot be clearly separated into the dichotomy of droplet *versus* airborne transmission (Bahl et al. 2020; Stadnytskyi et al. 2020). However, in health care facilities it is envisaged the adoption of precautions when aerosol-generating procedures are performed.

Exposure to contaminated fomites

A potential source of transmission is represented by indirect contact through fomites (i.e., inanimate surfaces and objects) contaminated by the hands of the infector or by the direct deposition of infective exhaled droplets. Otter et al. (2016) reported that SARS-CoVs inoculated on dry surfaces, show a 'dose response' in terms of survival, with more concentrated viral suspensions surviving longer than less concentrated suspensions.

In a food factory, surfaces are generally categorized into food contact and non-food contact surfaces. These inanimate surfaces include processing equipment, conveyor belts, electronics (touch screens and controls), furniture and other commonly touched items, such as counter tops, stairway rails, floors, walls, sinks and toilets. Employees getting in contact with infected surfaces and then touching their own eyes, nose or mouth can transfer the viral agent. As of 3th August 2020, SARS-CoV-2 transmission via inanimate surfaces has not been documented. In any case, work-related exposure can occur anytime in the food environment, especially in processing lines involving a high density of employees (e.g., manual sorting and packaging). van Doremalen et al. (2020) reported that SARS-CoV-2 is viable and infectious on surfaces up to days in the worst cases (depending on the inoculum shed), thus making fomite transmission of SARS-CoV-2 a plausible event. They evaluated the stability of the virus grown in tissue culture (at a concentration of 5.6 $\log_{10}$ $TCID_{50}$ per mL), after virus aerosolization, on different surfaces (at 23 °C and 40% final humidity). SARS-CoV-2 remained infectious for up to 4 hours on copper surfaces and up to 2-3 days on stainless steel and plastic. Under these conditions, the estimated half-lives on stainless steel and plastic were approximately 5.6 hours and 6.8 hours, respectively. Chin et al. (2020) investigated the stability of SARS-CoV-2-laden droplets (approximately 6.7 log $TCID_{50}$ per mL) on smooth surfaces at 22 °C. Under these conditions, SARS-CoV-2 was stable in a wide range (3–10) of pH values, whereas infectious virus was not detected on inoculated surfaces after four (plastic) or seven (stainless steel) days. Goldman (2020), by examination of reported studies on fomite transmission of COVID-19, referred that this route in real-life scenarios is unlikely, taking place only in instances where an infected person coughs or sneezes on the surface, and someone else touches that surface soon after the cough or sneeze (within 1–2 h).

Other transmission routes

SARS-CoV-2 has been revealed in blood samples and ocular secretions, but their contribution to the transmission of the infection is not clear (Tang et al. 2020; Young et al. 2020). Typically, respiratory viruses are not transmitted via blood, and in the case of SARS-CoV-2, despite of the theoretical risk, transfusion-transmitted infection has not been reported (Chang, Yan, and Wang 2020).

About 2-10% of confirmed COVID-19 cases showed diarrhoeal symptoms on the first days of hospitalization (Wang, Feng, et al. 2020). In a limited number of reports, viral RNA has been found in stool samples of infected patients (Holshue et al., 2020). Anyway, the detection of viral RNA does not inevitably indicate the presence of live virus in fecal matter and spread of COVID-19 through fecal-oral transmission (Bhowmick et al. 2020). Overall, there are no evidences of fecal-oral transmission, and the role of this route does not appear to be a driver in the spread of infection (Lai et al. 2020).

Moreover, waterborne transmission of SARS-CoV-2 was investigated as a hypothetical vehicle of contamination. To date no cases of spread through water for human consumption have been documented. Water suitable for human consumption is submitted to disinfection treatments to inactivate the more resistant non-enveloped enteric viruses, such as Adenovirus, Norovirus, Rotavirus and Hepatitis A virus. On these bases, it is likely that SARS-CoV-2 is inactivated too (Silverman and Boehm 2020). The mechanistic reasons for the higher susceptibility of enveloped viruses (in comparison to non-enveloped) to inactivation in aqueous environments are mostly unknown (Ye et al. 2018).

Establishing the relative contribution of each route of transmission in respiratory infectious illnesses is a difficult task, but it is important for an effective control. Gao et al. (2021) developed a multi-route mathematical model of respiratory infection. These authors considered in their model three transmission routes, i.e., the long-range airborne transmission, the respiratory close contact transmission (including short-range airborne transmission, direct inhalation of medium droplets or droplet nuclei < 100 μm in diameter), and the direct deposition of droplets of all sizes. They reported that all transmission routes could dominate under different exposure settings. This model dissipated the traditional dichotomy of respiratory infection being transmitted by either close-contact (i.e., direct spray route) or long-range airborne route, and it provided a basis for predicting the impact of individual level intervention methods, such as increasing close-contact distance and wearing protective masks.

Environmental factors affecting SARS-CoV-2 viability and transmission in the food factory

Typically, enveloped respiratory viruses do not survive very long in the environment. Their viability is a function of environmental conditions and virus structures (Ye et al. 2018). Differently, non-enveloped foodborne viruses, are less susceptible to environmental (temperature, light, pH), physical (desiccation) and biological (microbial antagonism) factors. Among the latter, Norovirus and Hepatitis A virus, which are the major causes of non-bacterial foodborne outbreaks, can survive on food and food contact surfaces for several days (Todd and Greig 2015). Their transmission occurs via fecal-oral route and in these cases, any food that has been handled manually is at risk for contamination, in particular the ready-to-eat foods are the most important cause of foodborne disease (Leon and Moe 2006). There is no evidence of viruses causing respiratory illnesses to be transmitted via food and it is "highly unlikely" that people can contract COVID-19 from food or food packaging (WHO-FAO 2020). Indeed, this route remains quite improbable when hygiene practices are correctly applied (BFR 2020; CDC 2020).

Relative humidity and temperature influence the kinetics of inactivation of HCoVs aerosolized in the environment (Chan et al. 2011). A novel inactivation model specific to the *Coronaviridae* family identified these two environmental parameters as major factors to predict infectious CoV persistence on fomites. Chin et al. (2020) by heating at 70 °C a liquid culture of SARS-CoV-2 in transport medium at a final concentration of 6.8 $\log_{10}$ $TCID_{50}$ per mL observed its inactivation within 5 min. In general, heat inactivation is an approach to minimize the risk of viral contamination for food. Inactivation data of viruses, including CoVs, in different matrices have been collected from empirical studies and used to develop mathematical models to predict virus inactivation as a function of temperature, time and RH (Guillier et al. 2020; Nims and Plavsic 2013). These models can be adopted to open the way to risk assessment for SARS-CoV-2.

On June 2020, lockdown measures were reintroduced in Beijing following a resurgence of COVID-19 outbreak in people working in a wholesale food market (Reuters 2020). The presence of the virus was revealed on various surfaces (in particular chopping boards) in the trading sections for meat and seafood. Authorities said that discovering the source of infection was a hard task and suspected the both the low temperature and the high humidity behaved as contributing factors. They hypothesized that cross-contamination phenomena were most likely involved. Over the world, nine clusters of COVID-19 linked to food processing plants have been identified (Leclerc et al. 2020). In particular, meat-processing plants emerged as incubators for the SARS-CoV-2 and the virus spread rapidly among workers. In these locations employees are involved in high levels of physical activity. Besides, cold, damp as well as lack of ventilation are conditions allowing the virus to survive longer on surfaces. In the US, among approximately 130,000 workers at meat and poultry processing lines, 4,913 encountered COVID-19 and 20 died to April 2020 (Dyal et al. 2020).

Prevention measures to SARS-CoV-2 transmission in food processing environments

The prevention of food contamination and the management of food safety risks requires the implementation food safety management systems based on the hazard analysis and critical control point (HACCP) principles (BFR 2020). As issued by EC Regulation n. 852 of 2004, the food industry adopts an approach based on prevention and control to maintain the integrity of the food chain, and to make available safe food supplies to the consumer. Hygienic production in food areas is ensured by several factors, including design of structures, zoning of processing areas, adequate sanitation procedures, engineering/maintenance of heating/ventilation/conditioning systems, fitness to work, good hygiene practices, and updated trainings on hygiene matters.

Policy guidelines to minimize the risk of COVID-19 infection in food factories

During the ongoing SARS-CoV-2 outbreak, international health authorities and food safety organizations enforced the adoption and implementation of hygiene and sanitation practices in the food industry. Center for Disease Prevention and Control (CDC) and Occupational Safety and Health Administration (OSHA) issued a guidance on the exposure risk among meat and poultry processing workers in the US (OSHA-CDC 2020). In these sectors, workers are exposed to SARS-CoV-2 not through the meat products they handle, but because they work in close proximity to each other. Factors affecting the risk of transmission include difficulties with workplace physical distancing and hygiene as well as crowded living and transportation conditions.

To carry out a workplace risk assessment for exposure to COVID-19, WHO defined three risk categories (low-, medium-, and high-risk exposure) planning for preventive measures (WHO 2020b). The food facility, involving working tasks with frequent contact among coworkers, customers or contractors, was categorized as a work activity with a medium-exposure risk. However, it was recognized that, in the same working scenario, there may be tasks with different levels of exposure. Consequently, the risk assessment should be carried out for each specific work setting (WHO 2020b). Several measures were suggested to prevent the transmission or exposure to the virus for food workers (Figure 1). The main recommended prevention strategy in a food processing environment is the physical distancing, which can be achieved by: *i)* adopting stagger workstations on either side of processing lines, so that food workers are not facing each other (at least 1 m apart for work stations and common spaces is advisable); *ii)* placing workers side-by-side rather than face-to-face; *iii)* developing a policy on wearing a face covering in line with national guidance; *iv)* spacing out

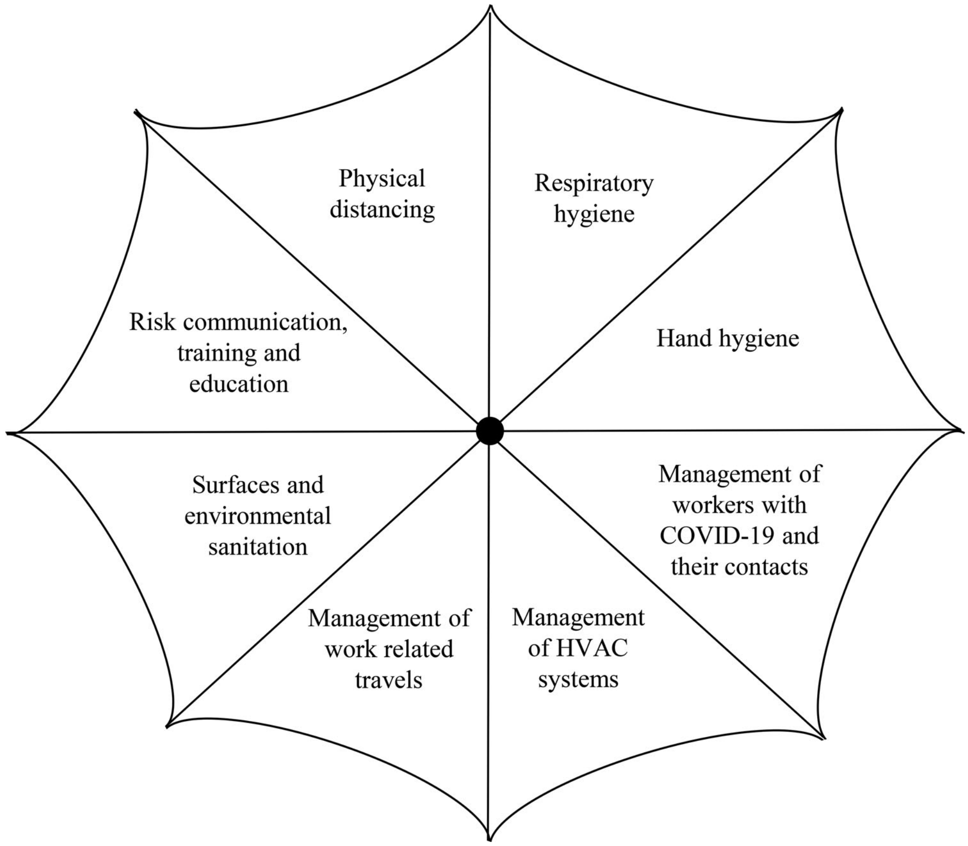

Figure 1. Measures, issued by the World Health Organization, to prevent the spreading of SARS-CoV-2 in workplaces.

workstations; *v)* limiting the number of workers in a food preparation area at any one time and *vi)* organizing workers into teams to promote reduced interaction between groups. Frequent and correct hand hygiene is suggested by international organizations to prevent infection with the SARS-CoV-2 (WHO-UNICEF 2020; WHO-WPR 2020). Hand hygiene stations should be close to the workplace and made accessible to all staff. In addition, respiratory hygiene is mandatory and respiratory etiquette by all working employees should be promoted. Wearing a mask must be in line with government guidance, and when used, it is necessary to ensure safe and proper use, care and disposal. Thermal screening should be considered as well. A refreshed training on food hygiene principles is necessary to reduce the risk of contamination of food surfaces. Additional preventive activities to be put forward include an enhanced sanitation of objects and surfaces regularly touched, not only along the processing lines but also in bathrooms and changing rooms.

Chemical sanitation

Despite the high transmission rate, SARS-CoV-2 is susceptible to the most common cleaning and disinfecting agents (Chin et al. 2020). Enveloped viruses are deemed to be more susceptible to disinfectants, but they may react differently than non-enveloped viruses with regard to the concentration and required application time of the active ingredient (Darnell et al. 2004; Eggers et al. 2015; Pfaff et al. 2019).

Hand hygiene by chemicals

Most of the literature on disinfectants for hand hygiene refers to studies carried out in the health care sector. These reports evaluate the effectiveness of broad spectrum active substances covering both non-enveloped and enveloped viruses, thus offering increased protection. Handwashing or use of a hand rub agent can reduce the levels of transient viruses both by inactivating and by physically removing them from the skin (Larson, Cohen, and Baxter 2012). The ideal disinfectant should be characterized by broad-spectrum biocidal activity, fast action, resistance to influence from the environment, non-toxicity and lack of equipment corrosion (Juszkiewicz et al. 2019). In a food factory, the SARS-CoV-2 transfer through employees' hands is a potential route of infection. Most biocidal products used in hand hygiene easily inactivate enveloped viruses (Ionidis et al. 2016). Alcohol-based hand-rubs inactivate enveloped viruses even in the presence of interfering organic loads (Kampf, Steinmann, and Rabenau 2007). The use of ethanol for hand rubbing is widespread. WHO proposed (for hand disinfection in the health care sector) two alcohol-based formulations characterized for their fast action, broad spectrum of microbicidal activity as well as easy accessibility and safety (WHO 2009). Formulation I contains ethanol (80% v/v), glycerol (1.45% v/v) and hydrogen peroxide (H_2O_2; 0.125% v/v), whereas formulation II contains isopropyl alcohol (75% v/v), glycerol (1.45% v/v) and H_2O_2 (0.125% v/v). Both solutions, through a quantitative suspension assay, were able to inactivate SARS-CoV within an exposure time of 30 s

(Siddharta et al. 2017). In detail, formulation II showed a higher virucidal activity, being capable to completely inactivate the virus at 30% biocidal concentration, whereas this evidence was reached with formulation I only at 40% concentration. Isopropanol, having one carbon more than ethanol, exhibit higher lipophilic properties and thus higher virucidal activity. Kratzel et al. (2020) tested different concentrations of WHO formulations in SARS-CoV-2 suspensions. The inactivation profile overlapped that of SARS-CoV. Also in this case, formulation II showed a better virucidal effect (in 30 s) at a minimal concentration of 30%. In the food industry frequent handwashing breaks the chain of contamination. Hand cleaning and disinfection are rapid actions taking place within approximately one minute. Terminal disinfection based on alcohols is recommended as a convenient alternative in the absence of soap and water. Other active substances used in hand disinfection with specific virucidal activity include chlorhexidine, olenaxidine gluconate (a biguanide derivative), povidone-iodine, other nitrogen-based substances, such as quaternary ammonium compounds, polybiguanide or their blends with alcohols (Eggers 2019; Eggers et al. 2018; Imai et al. 2020; Stanga 2010).

Environmental disinfection

As previously reported, SARS-CoV-2 may spread by droplets, travel for long periods and then settle, leading to fomite contamination. For this reason, environmental control methods including the cleaning and disinfection of contaminated surfaces and inanimate objects are a topic of interest (WHO 2014). Both food-contact surfaces and frequently touched surfaces require routine disinfection. In workplaces with suspected cases of COVID-19, WHO guidelines recommend the use of 0.1% sodium hypochlorite (bleach) or 70% ethanol-containing solutions for items that cannot tolerate bleach (WHO, 2020). Previous tests carried out on suspensions of SARS-CoV showed that sodium hypochlorite is effective at 0.05% (i.e., 500 ppm of available chlorine) after five minutes of contact (Lai, Cheng, and Lim 2005). European CDC recommends sodium hypochlorite at 0.05% for generic smooth surfaces (ECDC 2020 b). Recently, Krug et al. (2018) verified the use of two common disinfectants on surfaces contaminated by the enveloped African swine fever virus (a transboundary animal disease virus) in a pork-packing environment. This virus, a major concern to the meat industry, is capable of spreading via fomites. The authors reported that this infectious virus, dried in swine blood or meat juices on steel coupons, was not removed by disinfection, thus pointing out the need to physically remove contaminated swine excretions from surfaces prior to disinfection and to choose effective chemicals to ensure complete virus inactivation. In this case, sodium hypochlorite at 0.06% after 2 min of contact time allowed obtaining the classic 4-$\log_{10}$ reductions. The disinfection is more difficult when applied to hard porous surfaces. For instance, abovecited virus dried on birch coupons required sodium hypochlorite at 0.2% and 30 min of contact time to be inactivated (Krug et al. 2012).

Laboratory tests, dating back to the late ’80s, showed that also aldehydes, povidone-iodine and benzalkonium chloride are capable to inactivate several pathogenic CoVs (Saknimit et al. 1988; Sattar et al. 1989). To date, virucidal products for surface decontamination in the food industry include quaternary ammonium compounds (alkyl benzyl dimethylammonium chloride, ADBAC; didecyl-dimethylammonium chloride, DDAC) and hydrogen peroxide (Stanga 2010).

Complementary techniques to minimize the spread of SARS-CoV-2 in the air

Vaporization/aerosolization of H_2O_2

In the health care sector, the air treatment of hospital rooms by H_2O_2 fogging is currently recognized as an effective tool against nosocomial viruses (Pottage et al. 2010; Otter et al. 2020). Hydrogen peroxide is a biocide producing reactive hydroxyl radicals capable of damaging microbial cell components and rapidly degrading in contact with organic material.

In the food industry, fogging is generally categorized, on the base of droplet size, into atomization (or nebulization) and aerosolization (Stanga 2010). Atomization generates droplets with a diameter $> 30\,\mu$m resulting in short settling times and moistened surfaces. This technique is preferably adopted in wet areas. Differently, with aerosolization droplets of disinfectant show a medium size no wider than 5 μm, long suspension times and, in most cases, an electric charge as a consequence of friction during the aerosolization process. The ultrafine droplet size of the dry fog prevents it from condensing onto surfaces. Consequently, surfaces are not wetted, and for this reason, this application is also commonly referred to as “dry mist” technique. The treatment is performed in closed areas in the absence of personnel and food. The irritating property of H_2O_2 to the skin and the eyes varies with its concentration. The maximum allowable concentration, based on results from mice inhalation studies, suggest that 1 ppm (i.e., 1.4 mg m^{-3}) would be sufficient for protection against irritation (Gagnaire et al. 2002). The average limit of exposure to H_2O_2, recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) and calculated as a time weighted average over an eight-hour work shift is 1 ppm (ACGIH 2008).

For this reason, after aerosolization and elapsed the decay period, room ventilation is required to favor the catalytic decomposition of residual hydrogen peroxide to water and oxygen and the subsequent reentry of employees (Italian Ministry of Health, 2020) (Table 2). Aerosolization automatic devices available on the market differ for the nozzle engineering, the concentration of the active substance delivered, the homogeneity of vapor/aerosol produced and cost. Typically, automated systems are used in areas with high hygienic requirements such as portioning or packaging areas (Masotti et al. 2019). Taking into account the efficacy of H_2O_2 aerosolization systems in the health care sector to reduce the airborne viral load, the environmental

Table 2. Techniques (in addition to common sanitation) to minimize environmental contamination by SARS-CoV-2 and its spreading in the food industry.

System	Virucidal activity	Pros	Cons	Reference
Vaporization /aerosolization by H_2O_2	Yes	No by-products; homogeneous delivery; (semi)automated disinfection of closed areas; short cycle times	Post-treatment ventilation as safety measure; unoccupied premises; regulatory standards not established; use of chemicals	Brown and Wray 2014; Burfoot et al. 1999; Masotti et al. 2019; Stanga 2010
UV-C radiation	Yes	Automated room disinfection; short cycle times; shielded lamps for health safety; rapid time to access; no by-products	Biocidal efficacy lamp-device related; post-treatment ventilation as additional safety measure; cost of equipment	EU Directive 2006; Masotti et al. 2019; Weber et al. 2016
In-situ generated ozone	Yes	Broad-spectrum biocide; automated room disinfection; short cycle times; no by-products; low perceivable concentration	Cost of a built-in catalytic converter; corrosive toward plastic materials after long or repeated contact (cracking); unoccupied premises	Dubuis et al. 2020; Hudson, Sharma, and Vimalanathan 2009; Predmore et al. 2015; Stanga 2010; Yao et al. 2020
Heating, ventilation air-conditioning (HVAC) systems	No	Easy-to-organize measure; removal of particle-laden SARS-CoV-2; no additional maintenance costs for duct cleaning	No virus inactivation; energy costs for prolonged running times	ASHRAE 2020; Rehva 2020

vaporization/aerosolization of H_2O_2 within the food factory is suggested as an effective complementary strategy to the standard sanitation protocols (Pottage et al. 2010).

Ultraviolet germicidal radiation

Ultraviolet (UV) radiation in the region 100-280 nm (i.e., UV-C radiation), is used as germicidal air disinfection to control the airborne transmission of pathogenic microorganisms in high-risk settings (Walker and Ko 2007). Low-pressure mercury discharge lamps, emitting at 254 nm are commonly used. UV-C irradiation inactivates microorganisms by damaging their (deoxy)ribonucleic acid (Reed 2010). This radiation source can be used to disinfect water, air and surface. Surface irradiation is limited by micro-shadows and absorptive protective layers. This technology, in the health sector, is accomplished through several methods, namely, *i)* irradiation of the upper room air, *ii)* irradiation of the whole room (patient-free), and *iii)* irradiation of the air as it passes through enclosed-air circulation and heating, ventilation air-conditioning (HVAC) systems (Reed 2010). Recently, clinical trials demonstrated the effectiveness of an automated whole room UV-C disinfection system against MERS-CoV and SARS-CoV (Bedell, Adam, and Buchaklian 2016). The experiment was carried out on a surrogate model virus (i.e., mouse hepatitis virus strand A59) loaded on glass coverslips in UV permeable Petri dishes. Petri dishes were placed at 4 feet distance from the UV source. Plate counts indicated that MERS-CoV was reduced by 5.9 $\log_{10}$ cycles after 5 min exposure, whereas undetectable levels of mouse hepatitis virus were reached after 10 min. The efficacy of UV devices is a function of many parameters, including soil load, type of pathogen, intensity, dose, distance from the device, exposure time, direct line of sight from device or shaded exposure, lamp placement, room size and shape, and surface (Weber et al. 2016) (Table 2). Only a few of the UV devices commercially available have actually been studied to evaluate their effectiveness to inactivate health care-associated pathogens inoculated onto various test surfaces placed in hospital rooms. Tested energies, at exposure times of several tenths of minutes, ranged from 12,000 to 36,000 $\mu W\ cm^{-2}$ (Weber et al. 2016). Inactivation time is shortened by use of UV reflective wall paint of UV-C device. In the food industry, "in-duct" HVAC systems with UV-C lamps must be considered as a complementary strategy to conventional sanitation to limit infectious outbreaks. UV irradiation is mainly applied after the air passage through the HVAC air-handling ductwork (also commonly referred to as "in-duct" system) allowing an effective air microbial inactivation (Masotti et al. 2019). UV lamps prove to be very useful in air ducts and store rooms for seasoning, chilling, and drying when foods cannot be removed (e.g. cheese, salami, Parma ham) (Stanga 2010). In food production lines, there is not a safety impact for workers, because they are not exposed to high intensity radiation. Lamp locations and air movement patterns within a room need to be considered for optimal virucidal activity. To date, the use of UV-C lamps as air cleaner is normally an economically suitable solution for health care facilities.

In-situ generated ozone

Biocidal products are called *in-situ* generated when a specific device allows their production directly at the site of use. Ozone is easily generated from oxygen or air and it breaks down to oxygen with a half-life of about 20 min (± 10 min as a function of the environment) (Hudson, Sharma, and Vimalanathan 2009). Gaseous ozone is a strong oxidant agent with proved virucidal properties (Predmore et al. 2015). Due to the gaseous nature, ozone can penetrate all surfaces, including crevices, fixtures, and under-surfaces of equipment, much more efficiently than liquid sprays and aerosols. The inactivation mechanism involves the formation of free radical (hydroxyl radical, superoxide anion and hydroxyperoxyl radical) capable of damaging microbial structures.

Both in laboratory and in simulated field trials, ozone gas concentrations of 20-25 ppm (i.e., 40-50 mg m^{-3}) inactivated (non-)enveloped viruses by at least 3 $\log_{10}$ on hard and porous surfaces and in presence of biological fluids (Hudson, Sharma, and Vimalanathan 2009). Environmental conditions affect ozone efficacy. A higher humidity leads to a higher production of free radicals. Ozone used at a low concentration is a powerful disinfectant for airborne viruses when combined with a high RH (Dubuis et al. 2020). Ozone has the drawback that in the gaseous phase it is a potential injurious substance to humans. The immediately dangerous to life or health air concentration (IDLH) level for ozone is 5 ppm for humans (Dubuis et al. 2020). The threshold limit value of exposure was set to 0.1 ppm (by volume) under normal working conditions for 8 h daily, whereas the minimum perceived ozone odor is about ten-fold lower (0.01–0.02 ppm). To treat the air inside unoccupied hospital rooms ozone levels below 0.1 ppm may be feasible. According to the Quebec Occupational Health and Safety Organization, operating at concentrations below this level, respiratory protective equipment is not needed. However, foreseeing the potential risks to the health of employees, a continuous ozone analyzer triggering a general alarm as soon as the concentration of ozone exceeds 0.1 ppm in the ozonated room should be installed (Masotti et al. 2019) (Table 2). A built-in converter of residual ozone characterizes some devices currently available at the market.

To date, reports on SARS-CoV-2 inactivation through ozone generators are lacking. Yao et al. (2020), studying the influence of environmental parameters (temperature, RH and ozone levels) affecting airborne survival of SARS-CoV-2, observed that the spread of the virus was reduced by the increase of ambient ozone level from 48 to 95 μg m^{-3}. This evidence suggested that the use of ozone generators inside the hospital or other risky environments is a potential strategy to slow down the pandemic.

Heating, ventilation and air conditioning systems

COVID-19 transmission by droplets can be particularly effective in over-crowded working areas, especially in case of air stagnation (ECDC 2020a). Heating, ventilation and air conditioning systems provide indoor areas with comfortable conditions by filtering indoor and outdoor air, cooling/warming and dehumidification. HVAC systems can be configured in a variety of ways as a function of the expected number of users and the activity. International organizations dealing with building environmental control systems, such as the Federation of European Heating, Ventilation and Air Conditioning Associations and the American Society of Heating, Ventilating, and Air-Conditioning Engineers acknowledged the potential role of airborne transmission and recommended ventilation control measures accordingly (ASHRAE 2020; Rehva 2020). A general advice consists in supplying as much outside air as reasonably possible. Where and when feasible, window airing should be used to boost ventilation. Generally, CoVs are susceptible to RH exceeding 80% and a temperature above 30 °C (Rehva 2020). Thus, to maintain a work environment comfortable for employees (usually set at 20 to 30% RH and 21 to 23 °C), the adjustment of setpoints for humidification as well as for air-conditioning is not needed. Whether the HVAC system is equipped with a twin coil unit (or another heat recovery device) that guarantees 100% air separation between return and supply side, the spreading of the virus via heat recovery devices is not an issue (Rehva 2020). Avoid air recirculation and increase fresh air supply is the gold rule to prevent contamination and the virus spreading. Following these principles, the ventilation system does not represent a contamination source and no changes are needed to the usual duct cleaning and maintenance procedures. In modern ventilation systems, aggregates of SARS-CoV-2 particles are within the capture area of outdoor air filters. Thus, these filters must be replaced only following the scheduled lifetime. Overall, in connection with COVID-19, maintenance instructions of manufacturer should be strictly followed, and air recirculation is an option to be excluded as much as possible, being a probable aid for transmission (Morawska et al. 2020). In a food processing line, direct airflow should be diverted away from employees in close proximity to avoid the virus dispersion from infected subjects and to minimize the direction of sustained air flow for stationary workers (ECDC 2020a). A minimum number of air exchanges per h should be ensured, because increasing this number will reduce the risk of transmission in closed areas.

Conclusions

Transmission routes of SARS-CoV-2 via direct contact and indirectly via air represent a threat in the food factory. Closed workplaces, such as food processing lines, are environments that may be at increased risk for acquisition of respiratory infections. In particular, the meat and poultry industry, being crowded and with employees in close proximity, resulted in environments prone to the spreading of COVID-19 disease. Prompt actions to decrease risks to employees staying prolonged times in these environments are required. Multiple prevention measures are suggested to minimize the risks of contamination. Practical and economically feasible recommendations, to control these working areas, consist in optimizing facility services, in particular the operation of HVAC systems. The disinfection of food contact surfaces applying routine protocols are effective, due to the sensitivity of SARS-CoV-2 to biocidal molecules adopted in the food factories. For the safety of food and employees, air disinfection through complementary techniques (e.g. aerosolization of H_2O_2, UV-C radiation or *in-situ* ozone generation) is a feasible strategy, but its implementation must be properly carried out due to safety concerns of each technique.

Disclosure statement

The authors declare no conflict of interests.

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