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## Review Article

# Time course and epidemiological features of COVID-19 resurgence due to cold-chain food or packaging contamination



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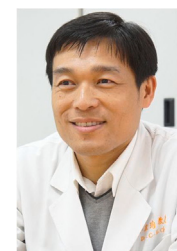
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## ABSTRACT

Contaminations in frozen food imported from countries with ongoing COVID-19 epidemics have been reported in China. However, the epidemiological features of the outbreaks initiated by material-to-human transmission were less reported. The risk of this route of transmission remains unclear, and strategies to prevent resurgence could be flawed.

We aimed to demonstrate the existence of cold-chain food or packaging contamination transmission and describe the time course and epidemiological features associated with the transmission in China. This review was based on the official reports or literature for resurging COVID-19 events that were related to cold-chain food or packaging contamination in China and other countries. Although SARS-CoV-2 on the material surface is not the main source of infection, the closed and humid environment for food packaging and transportation is a place favoring the material-to-human spread of SARS-CoV-2. In this transmission mode, patient zero is often hidden and difficult to detect, such that the outbreak usually can only be perceived after a period of a secret epidemic. Regular testing for high-risk populations and imported cold-chain products, proper disinfection of imported products, and protection of susceptible population while working remain an effective way to detect and prevent SARS-CoV-2 spread.

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Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, has become a global pandemic since early 2020 [1]. With strict nonpharmaceutical public health interventions, the local transmission of COVID-19 was contained in China; however, there have been small-scale outbreaks, especially in port cities, which was believed to be related to contaminated cold-chain food or materials, causing great concern in global. The report from WHO also mentioned the possibility of transmission of SARS-CoV-2 through frozen products [2]. The persistence, stability and infectivity of contaminated inanimate surfaces argued [3], to explore the indirect transmission routes of infection by fomite which was ignored.

COVID-19, is a respiratory infection, and the accepted route of transmission is respiratory droplets dispersed by coughing, sneezing, talking and singing or by the spread of aerosols. There is no evidence supporting that SARS-CoV-2 can follow the fecal-oral route, and the chance of foodborne transmission is extremely low [4]. However, the spread of SARS-CoV-2 particles from infected personnel to food packaging or to food surfaces is possible. While viruses are not able to propagate on the materials, these materials may work as a potential carrier for their spread. Transmission may occur indirectly through touching contaminated surfaces, followed by touching the mucosal membranes of mouth, nose, or eyes, and fomite transmission is possible [5]. We review the serial events in China after the main outbreak in Wuhan that related to contaminated frozen products and analyze relevant laboratory evidence support this hypothesis, hope to provide a few tips to strengthen the weak links of epidemic prevention and control.

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## Literature base

To clarify the possibility of cold-chain food or packaging contamination as a route of COVID-19 transmission, we performed a search on the official website of the Centers for Disease Control of China and local authorities ( <http://www.chinacdc.cn/en/> ) for resurgence events that related to cold-chain food or packaging contamination, and official reports or literature about traceability investigation.

We also conducted a literature and report search to assess the relevant epidemiological events and laboratory basis of this transmission route, to support the existence of such mode of transmission.

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## SARS-CoV-2 detection in cold-chain food products in China

Since July 2020, a series of incidents of imported frozen food as a carrier of SARS-CoV-2 have been reported in China, and most of the incidents were traced to frozen shrimp imported from Ecuador, where novel coronavirus was found not only on the outer packaging [6], but also on the inner packaging of frozen Pomfret from Ecuador [7].

On August 12, 2020, authorities in Shenzhen, Guangdong Province found SARS-CoV-2 on the surface of a frozen chicken

wing sample imported from Brazil [8], first time novel coronavirus was found on the surface of frozen food in China.

Both cases were confirmed by positive detection of nucleic acid, indicating the existence of the virus on the surface, but not truly indicating the presence of viable virus. Nevertheless, the event that occurred later in Qingdao, Shandong Province is different. On September 24, 2020, during a routine nucleic acid inspection of the personnel in Qingdao Port, two stevedores were found to be SARS-CoV-2 positive and considered asymptomatic patients without any contact history; later in the outbreak investigation, live virus was isolated from the outer packaging of imported frozen cold cod that was carried by the two stevedores [9]. This event became the first known case where the live SARS-CoV-2 was detected on cold-chain food in the world, confirming that SARS-CoV-2 can survive on the outer packaging for a long time under the condition of cold-chain transportation. This finding strongly supports the possibility of cold-chain foods as a vehicle of SARS-CoV-2 spread through cross-border transportation [10].

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## Virus survival on inanimate surfaces

In fact, as early as 1975, researchers have already found that viruses can survive long-term on common surfaces found in environments, and may play a role in virus transmission [11].

The recent studies also show that SARS-CoV-2 was detected from inanimate surface in the patient surroundings [12], another study shows unabsorbent materials like plastic are more dangerous than absorbent materials like cotton, because contaminated droplets are difficult to absorb [13]. Besides the effect of different types of materials, humidity and low temperature are more conducive to the survival of virus. SARS-CoV-2 was reported as being viable in aerosols for up to 3 h and on the surface of stainless steel and plastic for up to 2 and 3 days, respectively, at 21–23 °C and a relative humidity of 40% [14]. Another study showed that SARS-CoV-2 was stable on swine skin for at least 14 days at 4 °C [15]. Whether at 4 °C or –30 °C, refrigerated human milk did not significantly affect the SARS-CoV-2 infectious viral load over 48 h period [16]. The lifespan of SARS-CoV-2 at 50% humidity was longer than at 30% humidity [17]. To ensure the quality of cold-chain food, when stored, transported, or sold, low temperature must be maintained all the time, usually at or below –18 °C. Plastic is the most common material for outer packaging. The closed and humid environment for food packaging and transportation is a workplace favoring the spread of SARS-CoV-2 [18]. Given the reverse relationship between temperature and virus stability, all these factors create a favorable condition that can drastically prolong the survival of SARS-CoV-2. As mentioned above, the outbreak in Qingdao could prove this possibility.

The cold-chain food and their packing could be contaminated at any step of production and transportation, through droplets expelled from infected workers who do not have appropriate personal protection equipment, by coughing, sneezing, talking or even breathing.

## Contaminated cold-chain food—or packaging-associated outbreaks in China

On June 11, 2020, after 56 consecutive days of no local transmission events in Beijing, a 52-year-old man was diagnosed with COVID-19, without any contact or travel history. Epidemiological investigation identified the Xinfadi Market as the origin of the outbreak, and salmon imported from another country was considered the origin of the outbreak [19,20]. This is the first outbreaks in China after the main outbreak of COVID-19 in Wuhan that traced to the contaminated cold-chain food, and researchers realized the possibility of this transmission mode in the first time.

On July 22, 2020, after 111 consecutive days of no local transmission events in Dalian, Liaoning Province, an outbreak related to the seafood processing workshop of company broke out, 92 confirmed cases in total, and another 26 persons with asymptomatic infection were identified [21,22]. On November 7, Tianjin Municipality received notification from Dezhou City, Shandong Province that samples of the outer packaging of

imported frozen pork products shipped from Germany via Tianjin Port were positive for SARS-CoV-2 by RT-PCR. On November 10, another asymptomatic patient was identified during the universal testing for all workers of cold storage and cold-chain companies across the city [See Figs. 1 and 2]. A screening campaign was implemented, and a stevedore and a driver were positive in RT-PCR, both had participated in the transport of an infected batch of frozen products from the port [23,24]. Analyzing the links between the cases according to the SARS-CoV-2 sequences of the collected samples, the investigation showed that (i) the two virus strains isolated from two infected persons belonged to two different Europe clusters; (ii) one of the two cases led to an outbreak via human-to-human transmission; (iii) the other case was a source-unknown case without further human-to-human spread, indicating that this case was likely infected via a route of contact transmission [24,25]. The package surface of frozen pork knuckle from Germany was contaminated by frozen pig heads carrying SARS-CoV-2 from North America, and subsequently, a worker of a cold-chain food company who had no any travel history

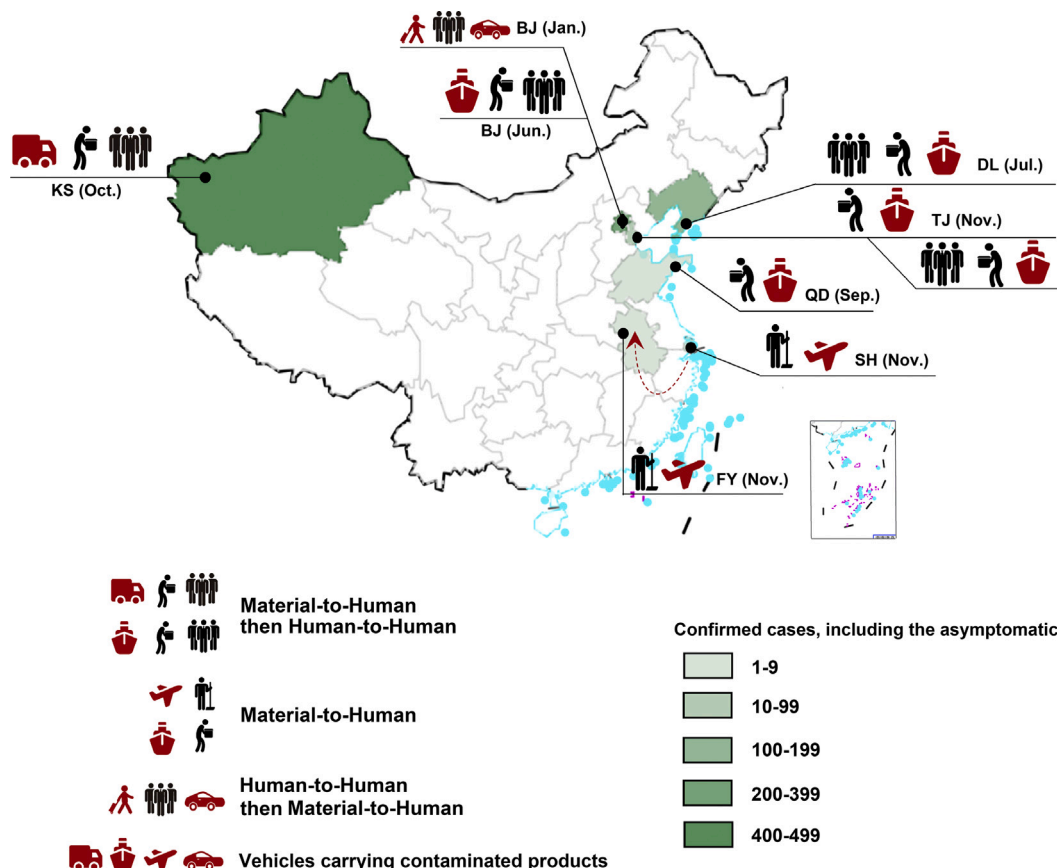


Fig. 1 Contaminated cold-chain food- or packaging-associated outbreaks in Mainland China, 2020. Regional distribution, scale and transmission mode of the identified outbreaks are demonstrated. Information was from published literature or compiled from official announcements or documents by local authorities. The vesicles that carried the contaminated products were mainly ships or cargo aircrafts in port cities; the outbreak in Kashgar was associated with a contaminated container in land transportation. Material-to-human transmission, with or without following human-to-human occurred in these outbreaks. The coastal regions and scattered islands are shown in light blue or pink color. The abbreviations are KS, Kashgar, Xinjiang Uygur Autonomous Region; BJ, Beijing; DL, Dalian, Liaoning Province; TJ, Tianjin; QD, Qingdao, Shandong Province; SH, Shanghai; and FY, Fuyang, Anhui Province.

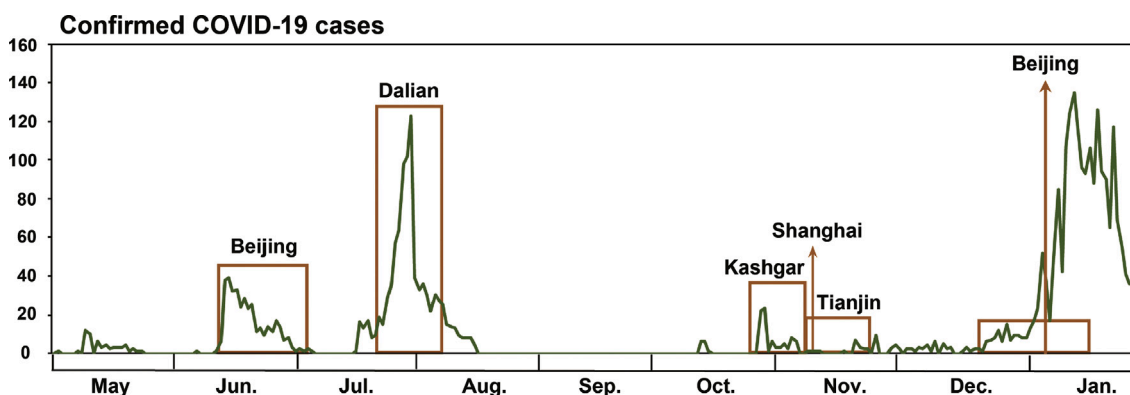


Fig. 2 Timeline of contaminated cold-chain food- or packaging-associated outbreaks in China, 2020. The number of confirmed COVID-19 cases, expressed in a green curve, represents the total number of newly diagnosed cases in China over time. Orange squares and arrows highlight the occurrence of the cold-chain food- or packaging-associated COVID-19 outbreaks in different cities in China. Only after the community outbreak is well controlled, then the hidden outbreak due to contaminated, imported cold-chain foods or food packaging can surface to be detected.

was suspected to be infected from the contaminated package [24,25].

Besides contaminated cold-chain food and packaging, contaminated object may also be a medium for virus transmission. On November 9th, a stevedore at Shanghai Pudong International Airport who had not recently had any contact with frozen foods, was diagnosed with COVID-19 [26]. According to the epidemiological investigation, the patient had entered to clean up an aircraft container transported from North America to Shanghai on October 30, without wore facial masks.

Recently on January 15, 2022, a local confirmed case was reported in Beijing without any contact or travel history. An international mail delivered from Canada on January 7 arrived in Beijing via the United States and Hong Kong, and the person who handled the mail on January 11 was infected. A total of 22 environmental specimens were collected, including the out and inner surface and papers inside the mail. All specimens were positive by PCR, and gene sequence analysis showed that the virus belonged to the VOC/Omicron variant (BA.1 evolutionary branch), highly similar to strains circulating in North America and Singapore in December 2021 [27].

Majority of the outbreaks in China could always be traced to the transmission chain originating from imported food products or mails to workers at market sites, seafood processing facilities, port cold storage, and postal mailing service [21–27]. Source of these infections was believed to be contaminated cold-chain food or materials, and it seems more dangerous because infectious SARS-CoV-2 has been reported to survive on the surface of cold-chain food packages for at least 60 days [28], and even longer at colder temperature and on extreme relative humidity (U-shaped dependence) [29]. With the occurrence of these outbreaks, we realized the existence of such a potential transmission route [See Figs. 1 and 2], and the corresponding prevention and control measures were come up with, and the scale of dissemination was gradually reduced.

### Similar events in other countries

On August 11, 2020, New Zealand announced four confirmed cases in one Auckland household after 102 consecutive days of no local transmission events. These cases had no overseas travel history, but one of them was the employee of a cold-chain company [30]. On August 13, another 13 newly confirmed cases were reported; 3 were employees at the same cold-chain company, and another 7 were family members of these employees. As of October 20, 2020, a total of 179 origin-unknown cases with a C.12 lineage of virus sequence have been reported, and designated as the outbreak of Auckland August Cluster [31]. Similar outbreaks occurred among workers at processing facilities for meat, poultry, seafood, fruit and vegetable were also observed in other countries, including Japan, Australia, Germany, England and Wales, and the United States [32].

In addition to SARS-CoV-2, norovirus have similar transmission. From July to October, 2019, there have been multiple cruise ship outbreaks of norovirus in the United States, after the review of food provisioning implicated the raspberries as the infection cause. Subsequently, frozen raspberries that can be traced back to China was recalled [33].

We have also noticed that food production workers might be at increased risk for SARS-CoV-2 infection because of their work [34]. Distinctive factors contributed to workplace transmission, including prolonged close contact with coworkers, shared work space, shared transportation and congregate housing [35]. The high-risk workplaces were meat and poultry processing facilities, which had the closest connection with cold-chain food [35,36]. According to the data released by the Centers for Disease Control and Prevention of the United States, during March 1 – May 31, 2020, there were 28,364 reported cases and 132 (0.5%) deaths among workers in 382 meat and poultry processing facilities in 31 states [37]. These workplaces were often crowded, and always with high humidity, which is an ideal environment

for SARS-CoV-2 to linger and spread. In the process of production and packaging, the virus might attach to the inner and outer packaging, even to food, and persist for a long time under the conditions of cold chain transportation. Under such circumstances, human-to-human, human-to-material, and material-to-human transmissions were all possible.

### Features of transmission

COVID-19 is a respiratory infection, virus could replicate in the upper respiratory tract, and shed high RNA copies to environment, especially in the first week of symptom onset [38,39]. SARS-CoV-2 is also considered to be more stable and persistent than other human coronaviruses in the environment [40]. The following conditions are required for contaminated cold-chain food or packaging to cause human infection. First, COVID-19 carrier could shed virus to surface; second, the virus is still alive after long distances transported, and can remain highly stable on material surfaces, such as card board and plastic, for days, particularly under refrigerated (4 °C) and frozen (−10 to −80 °C) conditions [41–43]; last, workers in wharf are infected through direct contact, and the virus once reach the human body, they can disseminate rapidly through human-to-human transmission [32].

In this review of the relevant outbreaks, patient zero was always the stevedore and usually asymptomatic. It is likely that the virus titer on the materials will gradually decline over time [29,43]. Infection due to direct contact with the contaminated material is often mild or asymptomatic, and therefore the patients may not be motivated to seek medical treatment in the beginning; however, they can become the source of infection, through human-to-human transmission, to other vulnerable individuals. Patient zero is often hidden and difficult to detect, and the outbreak can only be perceived after a period of a secret epidemic.

We realized that a positive nucleic acid testing does not necessarily mean the existence of an active transmission. On August 6, 2020, in Yingkou, Liaoning Province, three samples were found to be positive in the testing of outer packaging of the food products, but the nucleic acid as well as antibody testing on 43 employees and 306 related personnel of the enterprise were all negative [44]. To date, there have been no case reports of infection caused by eating or purchasing cold-chain products. According to the investigations of the outbreaks, the high-risk group is port staff, especially the stevedores, who may have direct contact with contaminated materials. Protecting workers from becoming infected with COVID-19 presents substantial challenges. These people should be placed on the top priority for immunization.

In response to changes in the transmission routes, the Joint Prevention and Control Mechanism of the State Council of the People's Republic of China promulgated a series of technical guidance at the national level for the prevention and control of COVID-19 transmission related to cold-chain food production in 2021 [45]. Benefitting from these policies, several outbreaks were detected before the occurrence of an epidemic.

### Summary

The focus of prevention and control therefore should not only focus on imported products but on the entire territory, not only on humans but also on materials. Our observations suggest that regular sampling and testing of high-risk groups and imported products and proper disinfection of imported products should be an effective way to detect and prevent the spread of the virus via such mode of transmission.

### Conflicts of interest

The authors have no conflicts of interest to declare.

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