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Natural Host–Environmental Media–Human: A New Potential Pathway of COVID-19 Outbreak

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ABSTRACT

Identifying the first infected case (patient zero) is key in tracing the origin of a virus; however, doing so is extremely challenging. Patient zero for coronavirus disease 2019 (COVID-19) is likely to be permanently unknown. Here, we propose a new viral transmission route by focusing on the environmental media containing viruses of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or RaTG3-related bat-borne coronavirus (Bat-CoV), which we term the "environmental quasi-host." We reason that the environmental quasi-host is likely to be a key node in helping recognize the origin of SARS-CoV-2; thus, SARS-CoV-2 might be transmitted along the route of natural host–environmental media–human. Reflecting upon viral outbreaks in the history of humanity, we realize that many epidemic events are caused by direct contact between humans and environmental media containing infectious viruses. Indeed, contacts between humans and environmental quasi-hosts are greatly increasing as the space of human activity incrementally overlaps with animals' living spaces, due to the rapid development and population growth of human society. Moreover, viruses can survive for a long time in environmental media. Therefore, we propose a new potential mechanism to trace the origin of the COVID-19 outbreak.

1. Introduction

In general, identifying the first infected case (patient zero) is key in tracing the origin of a virus; however, doing so is extremely challenging. Despite extensive efforts, scientists have not yet identified patient zero for the 1918 influenza pandemic, human immunodeficiency virus (HIV), or H1N1 influenza in 2009, and patient zero for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is likely to remain unidentified as well. The challenge in identifying the origin of SARS-CoV-2 is that a great deal of interdisciplinary research is required; in particular, if patient zero was asymptomatic or had very mild symptoms, he or she may not have seen a doctor or generated a medical record. As a result, patient zero could forever remain unidentified. Therefore, what roadmap could be followed to skip over patient zero while still recognizing the origin of the virus?

Here, we propose a new virus transmission route (Fig. 1) by focusing on environmental media containing viruses such as SARS-CoV-2 or RaTG3-related bat-borne coronavirus (Bat-CoV), hereafter termed as the "environmental quasi-host." We propose reasons why the environmental quasi-host is likely to be a key node in helping recognize the origin of SARS-CoV-2.

Viral transmission to humans occurs via natural host–human contact or environmental quasi-host–human contact, where the environmental quasi-host might be water, soil, or food contaminated by an animal host's urine, saliva, feces, or secretions. Many researchers believe that SARS-CoV-2 may have come from the wild animal market. Nevertheless, they have focused on the natural host–human pathway [1–3], while ignoring the natural host–environmental quasi-host–human pathway.

Is it possible that SARS-CoV-2 infected patient zero through contact with an environmental quasi-host? With rapid industrialization and globalization, contacts between humans and environmental quasi-hosts are greatly increasing, as human activity spaces strongly overlap with animals' living spaces. Moreover,

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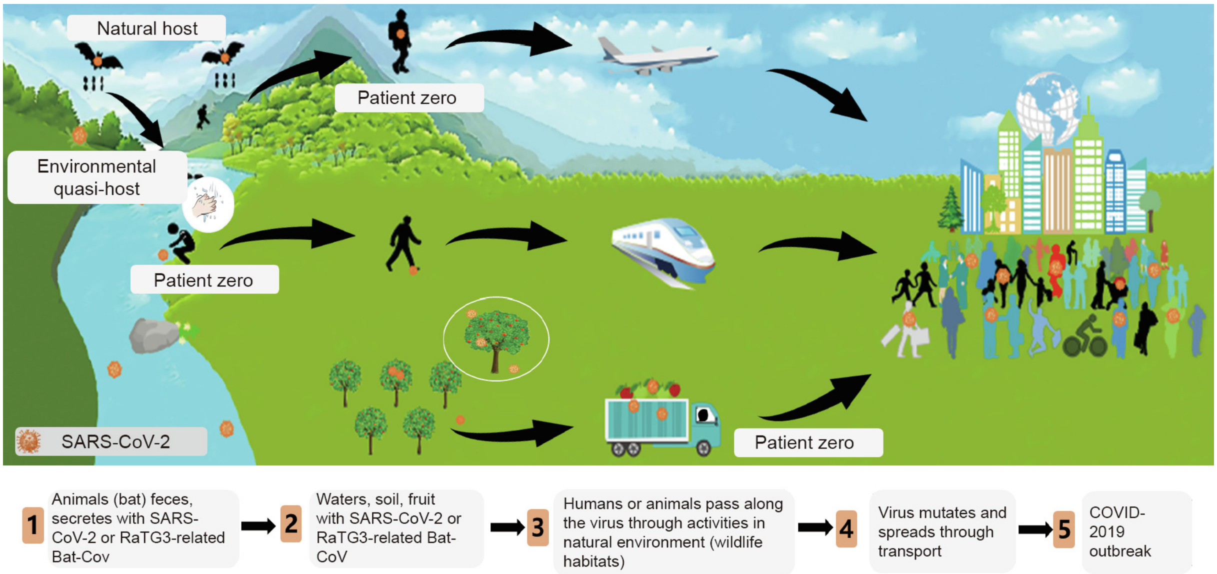

Fig. 1. The SARS-CoV-2 transmission pathway.

viruses can survive for a long time in certain environmental media [4–6]. Many viral outbreaks in humans have been caused by direct human contact with environmental media containing a virus, such as virus-carrying water and soil, rather than by direct contact with a natural host [7–10].

Based on the following pieces of evidence from recent research and other viral transmission pathways, we consider that SARS-CoV-2 could have been transmitted from an environmental quasi-host.

2. SARS-CoV-2 detection in various environmental media

SARS-CoV-2 has been detected in various environmental media (Table 1 [11–22]), including wastewater, soil, floor surfaces, door handles, sinks, lockers, tables, windows, and packages, to name just a few. Between February and March of 2020, Liu and colleagues [11] at Wuhan University in China demonstrated the presence of SARS-CoV-2 RNA in the air by setting up aerosol capture devices in and around two hospitals. Ong's group [12] detected SARS-CoV-2 on environmental surfaces in patients' rooms and toilets. SARS-CoV-2 has also been detected in wastewater at Schiphol Airport in Tilburg, the Netherlands [13]. SARS-CoV-2 may exist in the habitats of species that are natural hosts for SARS-CoV-2. Therefore, further examination of environmental media in natural habitats for SARS-CoV-2 is needed.

3. Long-term virus survival in environmental media

Viruses can survive in environmental media for hundreds or even thousands of days and remain infectious under suitable conditions, which are often reported to be low temperatures, relatively closed conditions, less disturbed conditions, and highly heterogeneous environmental media. *Mollivirus sibericum*, which has been preserved in permafrost for 30 000 years, is still capable of infection after resuscitation [23]. Porcine parvovirus can survive in soil for more than 43 weeks [6], and poliovirus remains stable and active at 1 °C for 75 days [24]. In groundwater, human norovirus still has 10% activity after 1266 days [25]. In mineral water, hepatitis A virus and poliovirus only have a small reduction in infectivity for one year at 4 °C [4]. In contaminated water, norovirus can still be detected after 1343 days [5].

We have analyzed 482 scholarly papers published in the past 120 years (Table 2 [26–122]), which study the survival time of 116 different strains of viruses. From a statistical perspective, over 84% of the 116 different strains of viruses can survive for more than one week (Fig. 2 [26–122]). With the rapid development of global transportation, viruses in environmental media can be carried from one place in the world to another in days or weeks; thus, the origin of a virus could be far away from the location of its breakout. As the phylogenetic characteristics of a virus may greatly affect its survival time in environment media, the phylogenetic characteristics of viruses require further study.

Table 1
SARS-CoV-2 detected in environmental media [11–22].

Environmental media	Collection period	Site or country	Reference
Aerosol	2020-02–2020-03	Wuhan, China	[11]
Wastewater	2019-11-27	Florianopolis, capital of Santa Catarina in southern Brazil	[14]
Wastewater	2019-12-18	Milan and Turin, Italy	[15]
Wastewater	2020-03-05–2020-04-23	Paris, France	[16]
Non-potable water	2020-04	Paris, France	[17]
Floor surfaces, door handles, sinks, lockers, tables, and windows	2020-01-24–2020-02-04	Singapore	[12]
Packages and the inner wall of a container of frozen shrimp	2020-07-03	Beijing, China	[18]
Samples from seafood, meat, and the external environment	2020-06	Beijing, China	[19]
Human feces	2020-01-01–2020-02-17	China	[20]
Human feces	2020	China	[21]
Wastewater	2020-02	Schiphol Airport in Tilburg, the Netherland	[13]
Soil and wastewater	2020-04	Wuhan, China	[22]

Table 2
Virus survival times in environmental media [26–122].

Virus survival time (t)	Viruses
t > 1 year	Reovirus [26], human adenoviruses [5], viral hemorrhagic septicemia virus (VHSV) [33], feline calicivirus (FCV) [36], calf rotavirus [26], poliovirus [4], hepatitis A virus (HAV) [4], tomato mosaic virus (TMV) [48], scrapie virus [52], H5N1 [56], H5N2 [60], H7N3 [60], H1N1 [65], H6N2 [69], H7N1 [71], marek's disease virus (MDV) [74], mouse hepatitis virus (MHV) [75], norwalk virus [5], granulosis virus [84], avian paramyxovirus-1 (APMV-1) [87], grapevine fanleaf virus (GFLV) [89], tomato ringspot virus (TmRSV) [92], human coronavirus 229E (HCoV-229E) [95], nuclear polyhedrosis virus (NPV) [96], African swine fever virus (ASFV) [98], swine vesicular disease virus (SVDV) [100], baculovirus midgut gland necrosis virus (BMNV) [102], granulosis viruses [Baculoviridae] [104], infectious hematopoietic necrosis virus (IHNV) [106], *Mollivirus sibericum* [23]
1 year > t > 1 month	Astrovirus (AstVs) [27], pike fry rhabdovirus (PFR) [30], spring viraemia of carp virus (SVCV) [30], infectious pancreatic necrosis virus (IPNV) [30], rotavirus [39], echovirus [42], Tulane virus (TV) [45], coxsackie virus [49], murine norovirus (MNV) [53], Ebola virus [57], H12N5 [61], H10N7 [61], H3N8 [66], H4N6 [66], H9N2 [72], transmissible gastroenteritis virus (TGEV) [75], hand foot mouth virus (FMDV) [78], koi herpesvirus (KHV) [81], snow mountain virus (SMV) [85], the minute virus of mice (MVM) [35], beet necrotic yellow vein virus (BNYVV) [90], salmonid alphavirus (SAV) [93], feline infectious peritonitis virus (FIPV) [95], variola virus [97], rhesus rotavirus (RRV) [99], frog virus 3 (FV3) [101], porcine teschovirus (PTV) [103], white spot syndrome virus (WSSV) [105], lymphocystis disease virus (LCDV) [107], neurovaccine virus [108], potato spindle tuber viroid (PSTVd) [62], prion [109], turkey reovirus (TRVs) [110], bovine parvovirus [111], bovine enterovirus [112], hepatitis E virus (HEV) [113], channel catfish virus (CCV) [114], avian reovirus [115], infectious salmon anemia virus (ISAV) [116], infectious pancreatic necrosis virus [117], parvovirus [118], duck plague herpesvirus [119], porcine parvovirus (PPV) [6], west Nile virus [120], H7N7 [121], hepatitis B virus (HBV) [122]
1 month > t > 1 week	H11N6 [28], human immunodeficiency virus (HIV) [31], equine herpesvirus type-1 (EHV-1) [34], porcine reproductive and respiratory syndrome virus (PRRSV) [37], human papillomavirus 16 (HPV16) [40], hepatitis C virus (HCV) [43], porcine sapovirus (SaV) [46], infectious bursal disease virus (IBDV) [50], Japanese encephalitis virus (JEV) [54], spumavirus [58], pepino mosaic virus (PepMV) [62], human parainfluenza viruses [63], lassa virus [67], venezuelan equine encephalitis virus (VEEV) [67], sindbis virus [67], taura syndrome virus (TSV) [76], severe acute respiratory syndrome coronavirus (SARS-CoV) [79], vesicular stomatitis virus (VSV) [82], nipah virus [86], hantavirus [88], severe fever with thrombocytopenia syndrome virus (SFTSV) [91], H3N2 [94]
t < 1 week	Simian virus 40 (SV40) [29], lung–eye–trachea virus (LETV) [32], herpes simplex virus (HSV) [35], feline leukemia virus (FeLV) [38], invertebrate iridescent virus 6 (IIV-6) [41], ostreid herpesvirus-1 (OsHV-1) [44], lapinized rinderpest virus [47], mouse rotavirus (MRV) [51], infectious bronchitis virus (IBV) [55], human polyomavirus (HPyVs) [59], potato virus Y (PVY) [62], suid herpesvirus-1 (SuHV-1) [64], human rhinovirus (HRV) [68], cytomegalovirus (CMV) [70], marburg virus [73], severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [77], measles virus [80], middle east respiratory syndrome coronavirus (MERS-CoV) [83]

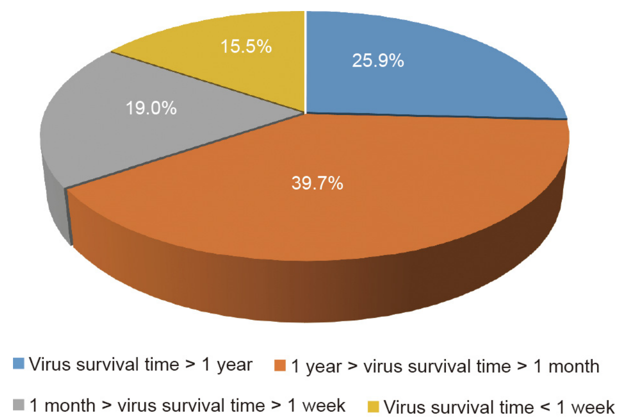

Fig. 2. The distribution of the survival times of the 116 studied viruses [26–122].

Existing studies have confirmed that SARS-CoV-2 is likely to exist for a long time in septic tanks and other soil-containing solid media, as well as in the ground [22]. The Singapore National Center for Infectious Diseases and the Defense Science Organization (DSO) National Laboratories have detected the virus in the residence rooms of COVID-2019 patients; floor surfaces had the highest positive viral signal, exceeding those of toilets, door handles, sinks, lockers, tables, and windows [12]. SARS-CoV-2 was found to remain viable in aerosols throughout the experiment (3 h), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ median tissue culture infective dose (TCID50) per liter of air [77]. Based on these findings, SARS-CoV-2 may exist and survive for a long time in habitat and activity place of wildlife, especially in places with low temperatures and low levels of light.

4. Viral outbreaks in humans caused by direct contact with environmental media rather than contact with a natural host

By analyzing the literature published in the past 120 years, we found at least 198 viral infection cases with 28 different strains of viruses that occurred through direct contact with environmental media (Table 3 [123–318]). Some of these cases were statistically derived from data in order to obtain a correlation between environmental media and viral transmission, and many were derived from investigations of environmental media that recognized the route or host of viral transmission. For example:

(1) A 44-year-old woman from Colorado, USA, suffered from Marburg disease in 2008 after returning home from a two-week tour in Uganda. This disease is caused by a virus that belongs to the same family as the Ebola virus, one of the deadliest pathogens to humans. Scientists sequenced the gene of an Egyptian fruit bat in a cave in Uganda and believed that she was infected by the virus when she touched a rock covered with bat feces while visiting the python cave [8–10].

(2) The transmission route of the Ebola virus has been confirmed as the human consumption of fruit contaminated by fruit bat feces [7].

(3) No less than five infectious disease incidents have occurred in China since 2009 due to drinking groundwater containing a virus that ended up affecting thousands of people. For example, an outbreak of gastroenteritis occurred in Hebei, China, in the winter of 2014–2015. The nucleotide sequence of the norovirus extracted from clinical and water samples had 99% homology with

Table 3
Cases of virus infection caused by direct human contact with environmental media [123–318].

Virus	The relevant environmental media	Site, region, or country	Date	Reference
Hepatitis E virus	Water	Kanpur, India	1991	[123]
	Water	Hyderabad, India	2005	[124]
	Water	Shimla, India	2015–2016	[125]
	Water	Am Timan, Chad	2016-09–2017-04	[126]
	Water	Hyderabad, India	2005-03–2005-08	[127]
	Water	Zhejiang, China	2014	[128]
	Surface water	Darfur, Sudan	2004	[129]
	Water	Abbottabad, Pakistan	1988	[130]
	Drinking water	Nepal	1995	[131]
Norovirus (Norwalk virus, a small round structured virus)	Groundwater, seawater	Italy	2003	[132]
	Water	Guatemala	2009	[133]
	Well water	Northeast Wisconsin, USA	2007-06	[134]
	Water	Switzerland	2008	[135]
	Drinking water	The Netherlands	2001-11–2001-12	[136]
	Drinking water	Iceland	2004	[137]
	Water	A ski resort in New Zealand	2006	[138]
	Water	Kilkis, Northern Greece	2012	[139]
	Drinking water, shower water	Western Norway	2002-07	[140]
	Lake water	Western Finland	2014-07	[141]
	Drinking water	Northern Italy	2009-06	[142]
	Water	Belgium	2007-07	[143]
	Water	Chalkidiki, Greece	2015-08	[144]
	Drinking water	Podgorica, Montenegro	2008-08	[145]
	Tap water	China	2010-10-31–2010-11-12	[146]
	Lake water	Maine beach, USA	2018	[147]
	Environmental surface	Colorado, USA	2019	[148]
	Food	A hospital and an attached long-term care facility (LTCF), Japan	2007	[149]
	Pork liver and lamb chops	Taiwan, China	2015-02	[150]
	Water or food contaminated with water	A cruise ship sailing along the Yangtze River, China	2014-04	[151]
	Sandwich	Hamilton County, Ohio, USA	1997	[152]
	Water	Wuhan, China	2017-04-28–2017-05-08	[153]
	Well water	Northwest University of China, China	2014-06	[154]
	Water	Salzburg, Austria	2005-05–2005-06	[155]
	Bottled water	Jiaxing, China	2014-02	[156]
	Water	South Africa	2017-01	[157]
	Bottled water	Catalonia, Spain	2016-04-11–2016-04-25	[158]
	Food	Shanghai, China	2012-12	[159]
	Recreational water	Netherlands	2002-06	[160]
	Drinking water	Northeast Greece	2006-06	[161]
	Well water	Xanthi, Northern Greece	2005	[162]
	Groundwater	Jeju Island, Republic of Korea	2004-05	[163]
	Food	Quebec, Canada	2011-01	[164]
	Food	Nagasaki, Japan	2003-11-18–2003-11-19	[165]
	Swimming pool water	Southeast England	2016-01	[166]
	Recreational water	Vermont, USA	2004-02	[167]
	Swimming pool water	Galveston County, Texas, USA	2013	[168]
	Recreational water	Puerto Rico	2009	[169]
	Air	Southern Sweden	2017–2018	[170]
	Air	Lianyungang, China	2017	[171]
	Ice	Taiwan, China	2015	[172]
	Food	Zhuhai, China	2011	[173]
	Food	Beijing, China	2017-12	[174]
	Water	Wuxi, China	2014-12-11	[175]
	Well water	Hebei, China	2014–2015	[176]
	Food	Shanghai, China	2013-12	[177]
	Food	Beijing, China	2018-09-04	[178]
	Food	Seven-day holiday cruise from Florida, USA to the Caribbean	2002-11	[179]
	Environmental surface	A 240-bed veterans LTCF, USA	2003-01–2003-02	[180]
	Well water	Sweden	Easter 2009	[181]
	Well water	Santo Stefano Quisquina, Sicily, Italy	2011-03	[182]
	Water	Nokia City, Finland	2007-11	[183]
	Ice	Delaware, USA	1987-09-19–1987-09-27	[184]

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Table 3 (*continued*)

Virus	The relevant environmental media	Site, region, or country	Date	Reference
	Food	Hamburg, Germany	2005-08	[185]
	Tap water	Hemiksem, Belgium	2010-12	[186]
	Environmental surface	An international cruise ship	2008	[187]
	Public toilet environment	Cruise ships	2005–2008	[188]
	Water, environmental surface	A cruise ship, Europe	Summer of 2006	[189]
	Dirty computer equipment (i.e., keyboard and mouse)	District of Columbia, USA	2007-02-08	[190]
	Environmental surface	Shanghai, China	2014-12-7–2014-12-18	[191]
	Food	A football game in the University of Florida, USA	1998-09	[192]
	Food	West Virginia, USA	2006-01	[193]
	Water	Shenzhen, China	2009-09-17–2009-10-03	[194]
	Food	Stockholm County, Sweden	2007-11	[195]
	Tap water	Taranto Bay, Southern Italy	2000-07	[196]
	Swimming pool water	Ohio, USA	1977-06	[197]
	Tap water	Heinävesi, Finland	1998-03	[198]
	Food	New York, USA	2000-02	[199]
	Drinking water	Northern Georgia, USA	1980-08	[200]
	Food	A hotel in Virginia, USA	2000-11	[201]
	Food	Virginia, USA	1999-05–1999-06	[202]
	Environment	Southern Finland	1999-12–2000-02	[203]
	Well water	Arizona, USA	1989-04-17–1989-05-01	[204]
	Water	Pennsylvania, USA	1978-07	[205]
	Aerosol	A primary school and nursery	2001-06	[206]
	Water	A ski resort in Sweden	2002-02–2002-03	[207]
	Food	Southern Sweden	2000-05-02–2000-05-03	[208]
	Food	Fort Bliss, El Paso, Texas, USA	1998-08-27–1998-09-01	[209]
	Aerosol	A large hotel, Canada	1998-12	[210]
	Water vapor	Ontinyent (Valencia), Spain	1992-01	[211]
	Recreational water	The Netherlands	2012-08	[212]
	Drinking water	Finland	1994-04	[213]
	Food (made from drinking water)	South Dakota, USA	1986-08-30–1986-08-31	[214]
	Water	North Georgia, USA	1982-01	[215]
	Water, food	Two Caribbean cruise ships	1986-04-26–1986-05-10	[216]
	Lake water	Markham County, Michigan, USA	1979-07-13–1979-07-16	[217]
	Food (exposure to non-drinking water)	The US Air Force Academy, USA		[218]
	Fomite	Sydney, Australia	2002-09	[219]
	Environment	North West England	1996-01–1996-05	[220]
	Food	Metropolitan Concert Hall, UK	1999-01	[221]
	Food	Toyota City, Japan	1989-03	[222]
	Food	A Massachusetts university, USA	1994-12	[223]
	Air	Los Angeles, USA	1988-12–1989-01	[224]
	Well water	A restaurant in the Yukon territory in Canada	1995	[225]
	Groundwater	La Neuveville, Switzerland	1998	[226]
	Tap water	A re-education ward	1999-01	[227]
	Food made from contaminated water	South Wales and Bristol, UK	1994-08	[228]
	Air	A British registered cruise ship	1988-01-13	[229]
	River water	Southern New South Wales, Australia	Christmas holiday period of 1989	[230]
	Raw oysters	Southwest Scotland	Christmas holiday period of 1993	[231]
	Aerosol	An elderly care unit, UK	1992-11	[232]
	Environment	A hospital for the mentally infirm, UK	1994-05	[233]
	Food	A large hotel, UK	1985-11	[234]
Hepatitis A virus	Drinking water	Mead County, Kentucky, USA	1982-11	[235]
	Well water	A trailer park in Bartow County, Georgia, USA	1982	[236]
	Lake water	Wateree Lake, USA	1969-09	[237]
	Water	Albania	2002-11–2003-01	[238]
	Bread	A village in South Cambridgeshire, England	The late spring and summer of 1989	[239]

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Table 3 (*continued*)

Virus	The relevant environmental media	Site, region, or country	Date	Reference
	Groundwater	USA	1971–2017	[240]
	Food	The Netherlands	2017	[241]
	Food	Italy	1996	[242]
	Shellfish	Shanghai, China	1988	[243]
	Well water	Guangxi, China	2012-05	[244]
	Food	Southern Italy	2002	[245]
	Groundwater	Thailand	2000	[246]
	Water	Rudraprayag District of Uttarakhand State, India	2013-05	[247]
	Water	Georgetown, Texas, USA	1980-06	[248]
	Frozen berries	Northern Italy	2013	[249]
	Clams	Valencia, Spain	1999	[250]
	Water	Orleans Island in the St. Lawrence River, Canada	Summer of 1995	[251]
	Swimming pool water	USA	1989	[252]
	Spa pool	Victoria, USA	1997	[253]
	Water	Republic of Korea	2015-04	[254]
	Water	Arapiles 62 camp located in Castellciutat, near Seo de Urgel, Spain	1987-09	[255]
	Drinking water	A medical college student's hostel, New Delhi, India	2014-01	[256]
	Orange juice	Europe	2004	[257]
	Frozen strawberries	Nordic countries	2012-10–2013-06-27	[258]
	Frozen mixed berries	Northern Italy	2013-01–2013-05	[259]
	Semi-dried tomato	The Netherlands	2010	[260]
	Pomegranate	USA	2013-05	[261]
Hepatitis C virus	Water	Medea, Algeria	1980–1981	[262]
	Wastewater	Sewage treatment plant, Algeria	1991	[263]
Parvovirus	Drinking water	USA	1971–1978	[264]
Measles virus	Air	The Minneapolis–St. Paul metropolitan area, USA	1991-07	[265]
Poliovirus	Milk	West coast of USA	1943-09	[266]
	Lake water	Oakland County, Michigan, USA	1993-06-11–1993-06-13	[267]
	Droplet	Middlesex Hospital, London, UK	Late summer of 1952	[268]
H5N1	Chicken manure	Indonesia	2005-06–2008-06	[269]
Rotavirus	Tap water	Isere region, France	1994	[270]
	Well water	India	2009-04–2009-05	[271]
	Water	Eagle-Vail, Colorado, USA	1981-03	[272]
	Aerosol	A primary school		[273]
Adenovirus	Swimming pool water	Oklahoma, USA	1982-07	[274]
	Environment	The marine corps recruit training command, San Diego, USA	2004	[275]
	Air	Wuhan, China	2014	[276]
	Swimming pool water	Georgia, USA	1977	[277]
	Swimming pool water	Beijing, China	2013	[278]
	Swimming facilities	Taiwan, China	2011-09	[279]
Hantavirus	Animal feces	North Dakota, USA	2016	[280]
	Deer mouse excreta	California, USA	2017	[281]
	Animal secretions	North Wales	2013	[282]
	Rat	Illinois and Wisconsin, USA	2017	[283]
SARS-CoV-2	Saliva	Hong Kong, China	2020	[284]
MERS-CoV	Camel	The United Arab Emirates	2019	[285]
	Droplet	Saudi Arabia	2013-03–2013-04	[286]
Severe fever with thrombocytopenia syndrome virus	Cat	Japan		[287]
Herpes simplex virus	Saliva	England	2019	[288]
SARS-CoV-1	Bat	Yunnan, China	2015	[289]
	Aerosol	Canada	2003	[290]
	Aerosol	Hong Kong, China	2003	[291]
	Air	Canada	2003	[292]
	Air	Hong Kong, China	2003	[293]
West Nile virus	Mosquito-controlled pool	California	2007	[294]
H3N2	Pig	Ohio, USA	2012	[295]
	Air, droplets	Alaska, USA	1977	[296]
H1N1	Droplet	Sichuan, China	2009	[297]
H7N7	Poultry, human	The Netherlands	2003-02	[298]

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Table 3 (*continued*)

Virus	The relevant environmental media	Site, region, or country	Date	Reference
Nipah virus	Raw date palm sap	Tangail District, Bangladesh	2004–2005	[299]
Hepatitis B virus	Foot care	Los Angeles, USA	2008	[300]
Human calicivirus	Well water	Wyoming, USA	2001-01	[301]
Echovirus	Swimming pool water	Kassel, Germany	2001-07–2001-10	[302]
	Swimming pool water	Rome, Italy	1997	[303]
Ebola virus	Body fluid	Congo	1995	[304]
	Body fluid	Congo	1995	[305]
Marburg virus	Bat or bat secretions	Uganda	2007-06–2007-09	[306]
	Bat or bat secretions	The Netherlands	2008	[307]
	Bat secretions	USA	2008	[308]
	Cave, mine, or similar habitat	Congo	1998-10	[309]
	Patient's body or secretion	Uganda	2012-09–2012-12	[310]
Enterovirus	Irrigation wastewater	Israel	1980–1981	[311]
	Drinking water	Switzerland	1998-08	[312]
	Seawater	Connecticut, USA	2004	[313]
	Food	England	2003-04	[314]
	Well water	Southern Missouri and Arkansas, USA	1978-05-07–1978-05-26	[315]
	Drinking water	Colorado, USA	1976-12	[316]
Hepatitis virus	Water	Austria	1952	[317]
	Water	France	1957-09-08–1957-10-05	[318]

the strain of Beijing/CHN/2015, which confirmed that the outbreak was waterborne. This is an excellent example of finding the route of virus transmission by investigating environmental media [154,176,194,244,319].

(4) Airborne transmission is an important mode of virus transmission, and at least six different cases of viruses infecting humans through airborne transmission have been reported. Alsved and colleagues took air samples from the surrounding environment of patients with norovirus infection and analyzed the norovirus RNA in the samples by reverse transcription polymerase chain reaction (RT-PCR). They detected norovirus RNA in some air samples, suggesting that air pollution from vomiting is an important source of norovirus [170,265,273,276,292,295].

Insights from a statistical perspective provide evidence for linkages between the environment and epidemics:

(1) Eight out of the 11 first reported human cases of Ebola occurred in areas with high levels of forest destruction, where the forests were the habitats of bats carrying the Ebola virus [320].

(2) The migration trajectory of ticks in damaged forest areas is significantly correlated to the distribution and morbidity of Kyasanur forest disease [321] and Lyme disease [322]. Moreover, habitat destruction increases both the survival pressure of wild animals and the viral load of urine and saliva secretions [323].

5. Viruses in many animals might transmit to humans through multiple pathways

The order Nidovirales, sub-family Orthocoronavirinae, family Coronaviridae is composed of four genera: α-coronavirus, β-coronavirus, γ-coronavirus, and δ-coronavirus. SARS-CoV-2 belongs to the subgenus *Sarbecovirus* of the genus β-coronavirus, to which SARS-CoV and MERS-CoV also belong. Coronaviruses (CoVs) infect humans as well as domestic and wild animal species, with infections remaining sub-clinical in most cases [324–326]. α-coronavirus and β-coronavirus usually infect mammals, with a probable origin of bats, while γ-coronavirus and δ-coronavirus mainly infect birds, and sometimes mammals, and might originate from swine [327–329]. A long list of animal species has been reported as intermediate hosts, such as dogs, cats, cattle, horses, camels, rodents, rabbits, pangolins, mink, snakes, frogs, marmots, hedgehogs, and ferrets [324,330–336]. Thus, there could be multiple viral transmission pathways from different animals to humans. The three outbreak points of coronavirus in China—namely, the livestock markets in Guangdong in 2003, the Huanan Seafood Market in Wuhan at the end of 2019, and the Xinfadi Seafood Market in Beijing in June 2020—are all related to animal markets. Civet cats and camels have been demonstrated to transmit SARS-CoV or MERS-CoV to humans, which provides an important hint of virus transmission directly from animals. However, it remains unclear which animal could be the main intermediate host of SARS-CoV-2, although positive viral RNA signals were detected in seafood markets and on the chopping boards of salmon. In 1983, Lidgerding and Hetrick [337] first reported the replication of a coronavirus in a fish cell line. Furthermore, Sano et al. [338] successfully isolated a coronavirus from common carp (*Cyprinus carpio*) in 1988, which induced hepatic, renal, and intestinal necrosis in experimentally infected fish. Miyazaki et al. [339] found a corona-like virus in color carp (*Cyprinus carpio*) in 2000, which caused dermal lesion and necrosis in internal organs.

Based on the aforementioned pieces of evidence, we propose that an environmental quasi-host can infect a human, and that there are two transmission routes of SARS-CoV-2:

(1) Natural hosts (animals with the virus)–environmental quasi-host (animal feces/water, soil and food contaminated by animals' urine, saliva, feces, and secretions)–patient zero (infected or virus-carrying human who came into contact with the environmental quasi-host while traveling or working in the wild)–back to home or human habitations–outbreak of COVID-19.

(2) Natural host (animals with the virus)–environmental quasi-host (fruit, food, or meat contaminated by animals' urine, saliva,

feces, and secretions)–transported to different regions or countries–patient zero (infected or virus-carrying human who came into contact with or ate the environmental quasi-host)–outbreak of COVID-19.

To summarize, it is imperative to investigate environmental quasi-hosts in order to source track the origin of SARS-CoV-2 through our two suggested transmission routes. Given the need to trace the virus around the world to prevent further pandemics, global collaboration is required not only to identify the origin of the virus, but also to fundamentally protect the existence and development of species. Doing so will proactively conserve and restore habitats for species, and serve as a key strategy for pre-empting the next pandemic.

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Compliance with ethics guidelines

Miao Li, Yunfeng Yang, Yun Lu, Dayi Zhang, Yi Liu, Xiaofeng Cui, Lei Yang, Ruiping Liu, Jianguo Liu, Guanghe Li, and Jiuhui Qu declare that they have no conflict of interest or financial conflicts to disclose.

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