DHS SCIENCE AND TECHNOLOGY

Master Question List for COVID-19 (caused by SARS-CoV-2)

Weekly Report

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For comments or questions related to the contents of this document, please contact the DHS S&T Hazard Awareness & Characterization Technology Center at HACTechnologyCenter@hq.dhs.gov.

Homeland Security

Science and Technology

DHS Science and Technology Directorate | MOBILIZING INNOVATION FOR A SECURE WORLD

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FOREWORD

The Department of Homeland Security (DHS) is paying close attention to the evolving Coronavirus Infectious Disease (COVID-19) situation in order to protect our nation. DHS is working very closely with the Centers for Disease Control and Prevention (CDC), other federal agencies, and public health officials to implement public health control measures related to travelers and materials crossing our borders from the affected regions.

Based on the response to a similar product generated in 2014 in response to the Ebolavirus outbreak in West Africa, the DHS Science and Technology Directorate (DHS S&T) developed the following "master question list" that quickly summarizes what is known, what additional information is needed, and who may be working to address such fundamental questions as, "What is the infectious dose?" and "How long does the virus persist in the environment?" The Master Question List (MQL) is intended to quickly present the current state of available information to government decision makers in the operational response to COVID-19 and allow structured and scientifically guided discussions across the federal government without burdening them with the need to review scientific reports, and to prevent duplication of efforts by highlighting and coordinating research.

The information contained in the following table has been assembled and evaluated by experts from publicly available sources to include reports and articles found in scientific and technical journals, selected sources on the internet, and various media reports. It is intended to serve as a "quick reference" tool and should not be regarded as comprehensive source of information, nor as necessarily representing the official policies, either expressed or implied, of the DHS or the U.S. Government. DHS does not endorse any products or commercial services mentioned in this document. All sources of the information provided are cited so that individual users of this document may independently evaluate the source of that information and its suitability for any particular use. This document is a "living document" that will be updated as needed when new information becomes available.

SARS-CoV-2 (COVID-19)	**Infectious Dose – How much agent will make a healthy individual ill?**	**Transmissibility – How does it spread from one host to another? How easily is it spread?**	**Host Range – How many species does it infect? Can it transfer from species to species?**
What do we know?	**The human infectious dose of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unknown by all exposure routes. SARS-CoV-2 is the cause of coronavirus disease 19 (COVID-19).** *Work using SARS-CoV-2* • A total dose of approximately 700,000 plaque-forming units (PFU) of the novel coronavirus SARS-CoV-2 was sufficient to infect cynomolgus macaques via combination intranasal and intratracheal exposure (10^6 $TCID_{50}$ total dose).[132] Macaques did not exhibit clinical symptoms, but shed virus from the nose and throat.[132] • Rhesus macaques are effectively infected with SARS-CoV-2 via the ocular conjunctival and intratracheal route at a dose of approximately 700,000 PFU (10^6 $TCID_{50}$).[59] • Rhesus macaques infected with 2,600,000 TCID50 of SARS-CoV-2 by the intranasal, intratracheal, oral, and ocular routes combined recapitulate moderate disease observed in the majority of human cases.[112] • Initial experiments suggest that SARS-CoV-2 can infect genetically modified mice containing the human ACE2 cell entry receptor; infection via the intranasal route (dose: 10^5 $TCID_{50}$, approximately 70,000 PFU) causes light infection, however no virus was isolated from infected animals, and PCR primers used do not align well with SARS-CoV-2, casting doubt on this study.[15] *Related Coronaviruses* • The infectious dose for severe acute respiratory syndrome coronavirus 1 (SARS) in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).[57-58] • Genetically modified mice exposed intranasally to doses of Middle East respiratory syndrome coronavirus (MERS) virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.[7, 48, 93, 174]	**SARS-CoV-2 is passed easily between humans, likely through close contact with relatively large droplets and possibly through smaller aerosolized particles.** • Pandemic COVID-19 has caused 838,061 infections and 41,261 deaths[80] in at least 180 countries and territories (as of 3/31/2020).[32, 137, 161] • In the US there are 177,452 confirmed SARS-CoV-2 cases across all 50 US states, with 3,440 deaths. (as of 3/31/2020)[80]; sustained community transmission of COVID-19 is occurring in the US.[18] • High-quality estimates of human transmissibility (R_0) range from 2.2 to 3.1[108, 118, 129, 167, 173] • SARS-CoV-2 is believed to spread through close contact and droplet transmission,[35] with fomite transmission likely[81] and close-contact aerosol transmission plausible[24, 71] but unconfirmed.[160] • SARS-CoV-2 replicates in the upper respiratory tract (e.g., throat), and infectious virus is detectable in throat and lung tissue for at least 8 days.[163] • Aerosolized virus has been detected in COVID-19 patient rooms, with particle sizes within the human respirable range (0.25 – 2.5 µm).[103] • SARS-CoV-2 is present in infected patient saliva,[149] lower respiratory sputum,[155] and feces.[97] **Individuals can transmit SARS-CoV-2 to others before they have symptoms.** • Pre-symptomatic[176] or asymptomatic[13] patients can transmit SARS-CoV-2; between 12%[62] and 23%[102] of infections may be caused by asymptomatic or pre-symptomatic transmission. • Severe cases are more likely to transmit disease; most new infections are within households of infected patients.[106] **Undetected cases play a major role in transmission.** • Models suggest up to 86% of early COVID-19 cases in China were undetected, and these infections were the source for 79% of reported cases.[95] **Behavior changes may limit spread.**[69] • Social distancing and other policies are estimated to have reduced COVID-19 spread by 44% in Hong Kong[54] and reduced spread in China.[84] • Modeling suggests that premature lifting of social distancing measures will substantially increase the number of local COVID-19 cases.[119]	**SARS-CoV-2 is closely related to other coronaviruses circulating in bats in Southeast Asia. Previous coronaviruses have passed through an intermediate mammal host before infecting humans; the identity of the SARS-CoV-2 intermediate host is unknown.** • Early genomic analysis indicates similarity to SARS-CoV-1,[179] with a suggested bat origin.[5,49, 179] • Positive samples from the South China Seafood Market strongly suggests a wildlife source,[37] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.[19, 50, 168, 172] • Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[131] The identity of the intermediate host remains unknown.[96, 99-100] • Viruses similar to SARS-CoV-2 were present in pangolin samples collected several years ago.[88] **SARS-CoV-2 uses the same receptor for cell entry as the SARS-CoV-1 coronavirus that circulated in 2002/2003.** • Experiments show that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS-CoV-1,[166] potentially explaining its high transmissibility; the same work suggests that differences between SARS-CoV-2 and SARS-CoV-1 Spike proteins may limit the therapeutic ability of SARS antibody treatments.[166] • Modeling of SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.[153] • There is currently no evidence that SARS-CoV-2 infects domestic animals or livestock.[78]

SARS-CoV-2 (COVID-19)	Infectious Dose – How much agent will make a healthy individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host Range – How many species does it infect? Can it transfer from species to species?
What do we need to know?	**Identifying the infectious dose for humans by any exposure route will facilitate model development; animal studies are a plausible surrogate.** • Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route	**Identifying the contribution of asymptomatic or pre-symptomatic transmission is important for implementing control measures. Additionally, the relative contribution of different infection sources – fomites, droplets, aerosols, and potentially feces – are unknown.** • Capability of SARS-CoV-2 to be transmitted by contact with fomites (phones, doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R_0) as control measures take effect • What is the underreporting rate?[79] • Can individuals become re-infected with SARS-CoV-2? • What is the difference in transmissibility among countries? • Is the R_0 estimate higher in healthcare or long-term care facilities? • How effective are social distancing measures? • When will infections peak in various cities and countries?	**Little is known about SARS-CoV-2 in non-human hosts.** • What is the intermediate host(s)? • What are the mutations in SARS-CoV-2 that allowed human infection and transmission? • What animals can SARS-CoV-2 infect (e.g., pet dogs, potential wildlife reservoirs)?

SARS-CoV-2 (COVID-19)	Incubation Period – How long after infection do symptoms appear? Are people infectious during this time?	Clinical Presentation – What are the signs and symptoms of an infected person?	Clinical Diagnosis – Are there tools to diagnose infected individuals? When during infection are they effective?
What do we know?	**The majority of individuals develop symptoms within 14 days of exposure. For most people, it takes at least 2 days to develop symptoms, and on average symptoms develop 5 days after exposure. Some individuals never develop symptoms but can still transmit disease.** • The best current estimate of the COVID-19 incubation period is 5.1 days, with 99% of individuals exhibiting symptoms within 14 days of exposure.[91] Fewer than 2.5% of infected individuals show symptoms sooner than 2 days after exposure.[91] • Individuals can test positive for COVID-19 even if they lack clinical symptoms.[13, 39, 72, 145, 176] • Individuals can be infectious while asymptomatic[35, 133, 145, 176]; and asymptomatic individuals can have similar amounts of virus in their nose and throat as symptomatic individuals.[180] • Infectious period is unknown, but possibly up to 10-14 days. [5, 95, 137] • On average, there are approximately 4[62] to 7.5[94] days between symptom onset in successive cases of a single transmission chain. • Most hospitalized individuals are admitted within 8-14 days of symptom onset.[178] • Patients can test positive via PCR for up to 37 days after symptoms appear.[178] Patients can test positive after recovery and hospital discharge.[89] The ability of these individuals to infect others is unknown. **Currently, there is no evidence that recovered patients can be reinfected with SARS-CoV-2.** • Experimentally infected macaques were not capable of being reinfected after their primary infection resolved.[14] • According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.[90]	**Most COVID-19 cases are mild, but severe disease can be found in any age group. Older individuals and those with underlying medical conditions are at higher risk of serious illness and death.** • The majority of COVID-19 cases are mild (81%, N = 44,000 cases)[145] • Initial COVID-19 symptoms include fever (87.9% overall, but only 44% - 52% present with fever initially[12, 72]), cough (67.7%[72]), fatigue, shortness of breath, headache, and reduced lymphocyte count.[36, 42, 76] Headache[41] and diarrhea are uncommon,[76, 94] though lack of appetite may be an early symptom.[117] • Complications include acute respiratory distress (ARDS, 17-29% of hospitalized patients,[45, 76] leading to death in 4-15% of cases[45, 76, 154]), pneumonia,[116] cardiac injury (20%[141]), secondary infection, kidney failure, arrhythmia, sepsis, and shock.[72,76,154,178] • Most deaths are caused by respiratory failure or respiratory failure combined with myocardial (heart) damage.[134] • Approximately 15% of hospitalized patients are classified as severe,[72, 145] and approximately 5% of patients are admitted to the ICU.[72, 145] • Current modeling suggests the overall case fatality rate (CFR) of COVID-19 is approximately 2.4%.[11] • The CFR depends on comorbidities; cardiovascular disease, hypertension, diabetes, and respiratory conditions all increase the CFR.[145, 178] • The CFR increases with age; individuals >60 are at higher risk of death,[145, 178] and >60% of confirmed fatalities have been male.[145] In the US, 34% of hospitalizations have been individuals younger than 44 years old.[4] • Variation in the CFR between countries may be due to demographics, testing criteria, and how COVID-19 related deaths are defined.[114] • Children of all ages are susceptible to COVID-19,[61] though generally show milder[43, 105] or no symptoms; up to 28% of children may be asymptomatic.[121] • Severe symptoms in children are possible,[101] and infant deaths have been recorded.[26, 105] • Based on one patient, a productive immune response is generated and sustained for at least 7 days.[146]	**Diagnosis relies on identifying the genetic signature of the virus in patient nose, throat, or sputum samples. These tests are relatively accurate. Confirmed cases are still underreported.** • US CDC has expanded patient testing criteria to include symptomatic patients at clinician discretion.[17] • PCR protocols and primers have been widely shared internationally.[31, 52, 94, 140, 157, 162] PCR-based diagnostic assays are unable to differentiate between active and inactive virus. • A combination of pharyngeal (throat) RT-PCR and chest tomography are the most effective diagnostic criteria (correctly diagnose 91.9% of infections).[126] A single throat swab detects 78.2% of infections; duplicate tests identify 86.2% of infections.[126] • Nasal and pharyngeal swabs may be less effective as diagnostic specimens than sputum and bronchoalveolar lavage fluid.[155] • RT-PCR tests can identify asymptomatic cases; SARS-CoV-2 infection was identified in 2/114 individuals cleared by clinical assessment.[75] • Combination RT-PCR and serology (antibody) testing may increase the ability to diagnose patients with mild symptoms, or identify patients at higher risk of severe disease.[175] • The FDA released an Emergency Use Authorization enabling laboratories to develop and use tests in-house for patient diagnosis.[68] • Updated tests from the US CDC are available to states.[31, 35] • Multiple rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,[55] BGI,[21] Cepheid[152], Abbot,[66] and Mesa Biotech.[22] • The US CDC is developing serological tests to determine what proportion of the population has been exposed to SARS-CoV-2.[83] • Machine learning tools are being developed to predict severe and fatal COVID-19 cases based on CT scans.[142]

SARS-CoV-2 (COVID-19)	Incubation Period – How long after infection do symptoms appear? Are people infectious during this time?	Clinical Presentation – What are the signs and symptoms of an infected person?	Clinical Diagnosis – Are there tools to diagnose infected individuals? When during infection are they effective?
What do we need to know?	**While the incubation period is well-characterized, less is known about how long individuals are infectious before, during, and after symptoms. Additionally, the possibility of reinfection warrants more research.** • What is the average infectious period during which individuals can transmit the disease? • Are individuals infectious after hospital discharge and clinical recovery, or are positive PCR tests only detecting non-infectious virus? • Can individuals become re-infected after recovery? If so, how long after?	**The true case fatality rate is unknown, as the exact number of cases is uncertain. Testing priorities and case definitions vary by location** • How long does it take for infected individuals to recover outside of a healthcare setting? • Are reductions in CFR through time (e.g., China) an indication of better treatment, less overcrowding, or both? • Are pregnant women at greater risk of complications during labor?[98] • How prevalent is loss of smell, loss of taste and gastrointestinal symptoms in COVID-19 patients?	**In general, PCR tests appear to be sensitive and specific, though robust estimates of false positive/negative rates are still lacking.** • False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual • With limited testing in many locations, how accurate are clinical diagnoses compared to genetic tests?

SARS-CoV-2 (COVID-19)	Medical Treatment – Are there effective treatments? Vaccines?	Environmental Stability – How long does the agent live in the environment?	Decontamination – What are effective methods to kill the agent in the environment?
What do we know?	**Treatment for COVID-19 is primarily supportive care including ventilation if necessary.**[72, 109] **A number of therapeutic trials are ongoing, but results are preliminary.**[20] **Convalescent sera is being tested at multiple sites across the US.**[110] • Two WHO global clinical trials are starting: Solidarity and Discovery.[86] These trials include remdesivir, hydroxychloroquine and chloroquine, ritonavir/lopinavir, and ritonavir/lopinavir and interferon-beta.[86] • Limited, preliminary evidence from clinical trials supports the efficacy of favipiravir,[44] tocilizumab,[169] intravenous immunoglobulin,[28] and hydroxychloroquine with azithromycin.[70] *Additional work is necessary to confirm therapeutic efficacy of any of these compounds.* • Limited, preliminary evidence shows mixed efficacy of chloroquine alone,[1] and no efficacy from combination ritonavir and lopinavir.[27] *Additional work is necessary to confirm the lack of efficacy of any of these treatments.* • Teams across the USA are testing passive antibody therapy (convalescent serum[29]) to patients (FDA Investigational New Drug approval).[67] In a small trial (5 patients), convalescent sera administration was followed by clinical improvement.[139] • Corticosteroids are commonly given to COVID-19 patients[178] at risk of ARDS,[170] but their use is not recommended by the US CDC.[33] • Laboratory testing identified 17 repurposed drugs with significant antiviral activity; more research is needed to confirm efficacy.[156] **Work is ongoing to develop a SARS-CoV-2 vaccine in human and animal trials. No preliminary results are available.** • Multiple entities are working to produce a SARS-CoV-2 vaccine,[8] including HHS/NIH/NIAID,[73, 92] Moderna Therapeutics and Gilead Sciences,[2-3, 113] Sanofi,[23] and Johnson and Johnson.[82] Moderna has begun phase 1 clinical vaccine trials in humans in WA state.[130] • CEPI has partnered with multiple entities to develop vaccines including University of Oxford, Novavax Hong Kong University, and the Institut Pasteur.	**SARS-CoV-2 can persist on surfaces for at least 3 days and on the surface of a surgical mask for up to 7 days depending on conditions. If aerosolized intentionally, SARS-CoV-2 is stable for at least several hours. The seasonality of COVID-19 transmission is unknown.** *SARS-CoV-2 Data* • SARS-CoV-2 can persist on plastic and metal surfaces between 3 days (21-23°C, 40% RH)[150] and 7 days (22°C, 65%RH). Infectious virus can be recovered from a surgical mask after 7 days (22°C, 65% RH).[46] • SARS-CoV-2 has an aerosol half-life of 2.7 hours (particles <5 µm, tested at 21-23°C and 65% RH).[150] • SARS-CoV-2 is susceptible to heat treatment (70°C), but can persist for at least two weeks at refrigerated temperatures (4°C).[46] • SARS-CoV-2 genetic material (RNA) was detected in symptomatic and asymptomatic cruise ship passenger rooms up to 17 days after cabins were vacated; the infectiousness of this material is not known.[111] *Surrogate Coronavirus data*: • Studies suggest that other coronaviruses can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)[30, 40], and porous surfaces for up to 3-5 days (SARS-CoV)[64] in air conditioned environments (20-25°C, 40-50% RH). • Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[30, 40, 123, 151] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[151]. • SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.[30] • No strong evidence exists showing reduction in transmission with seasonal increase in temperature and humidity.[107] • One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)[120] • Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.[87]	**Soap and water, as well as common alcohol and chlorine-based cleaners, hand sanitizers, and disinfectants are effective at inactivating SARS-CoV-2 on hands and surfaces.** *SARS-CoV-2* • Alcohol-based hand rubs are effective at inactivating SARS-CoV-2.[85] • Chlorine bleach (1%, 2%), 70% ethanol and 0.05% chlorhexidine are effective against live virus in lab tests.[46] • Twice-daily cleaning with sodium dichloroisocyanurate decontaminated surfaces in COVID-19 patient hospital rooms.[115] • EPA has released a list of SARS-CoV-2 disinfectants, but solutions were not tested on live virus.[6] *Other Coronaviruses* • Chlorine-based[159] and ethanol-based[51] solutions are recommended. • Heat treatment (56°C) is sufficient to kill coronaviruses,[123, 177] though effectiveness depends partly on protein in the sample.[123] • 70% ethanol, 50% isopropanol, sodium hypochlorite [0.02% bleach], and UV radiation can inactivate several coronaviruses (MHV and CCV).[135] • Ethanol-based biocides effectively disinfectant coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.[77, 164] • Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.[122] • Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.[147-148] • Coronaviruses are more stable in matrixes such as respiratory sputum.[63] • Hydrogen peroxide vapor can repeatedly decontaminate N95 respirators.[128] Devices capable of decontaminating 80,000 masks per day have been granted emergency use authorization from the FDA.[65]

SARS-CoV-2 (COVID-19)	**Medical Treatment – Are there effective treatments? Vaccines?**	**Environmental Stability – How long does the agent live in the environment?**	**Decontamination – What are effective methods to kill the agent in the environment?**
What do we need to know?	**In general, the efficacy of various therapeutic options for COVID-19 is unknown, though clinical trial results are beginning to be released.** • Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?[138] • Is the GLS-5000 MERS vaccine[171] cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS[53, 144] and MERS[38] • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics? • Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?[16]	**Additional testing on SARS-CoV-2, not surrogate viruses, is needed to support initial estimates of stability.** • Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)? • Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)	**Additional decontamination studies, particularly with regard to PPE and other items in short supply, are needed.** • What is the minimal contact time for disinfectants? • Does contamination with human fluids/waste alter disinfectant efficacy profiles? • How effective is air filtration at reducing transmission in healthcare, airplanes and public spaces? • Are landfills and wastewater treatment plants effective at inactivating SARS-CoV-2? • Is heat or UV decontamination effective to clean N95 respirators and other types of PPE for multi-use?

SARS-CoV-2 (COVID-19)	PPE – What PPE is effective, and who should be using it?	Forensics – Natural vs intentional use? Tests to be used for attribution.	Genomics – How does the disease agent compare to previous strains?
What do we know?	**The effectiveness of PPE for SARS-CoV-2 is currently unknown, and data from other related coronaviruses are used for guidance. Healthcare workers are at high risk of acquiring COVID-19, even with recommended PPE.** • Healthcare worker illnesses (over 1,000[145]) demonstrates human-to-human transmission despite isolation, PPE, and infection control.[136] • Risk of transmission to healthcare workers appears high, with up to 20% of healthcare workers in Lombardy, Italy becoming infected.[125] • "Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)"[34] • WHO indicates healthcare workers should wear clean long-sleeve gowns as well as gloves.[158] • Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols[159]; additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation).[25] • Particular attention should be paid to the potential for transmission via exhaled air during supportive respiratory procedures.[71] • There is evidence both for[103] and against[115] the detection of SARS-CoV-2 RNA via air sampling in patient rooms and other hospital areas. • The efficacy of "homemade" PPE, made with T-shirts, bandanas, similar materials, is less than standard PPE, but may be used if no other options are available.[47, 56, 127]	**All current evidence supports the natural emergence of SARS-CoV-2 via a bat and possible intermediate mammal species.** • Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat coronaviruses. The SARS-CoV-2 virus is distinct from SARS-CoV-1 and MERS viruses.[60] • Genomic analysis suggests that SARS-CoV-2 is a natural variant and is unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.[9, 179] • Genomic data support at least two plausible origins of SARS-CoV-2: "(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer."[9] Either scenario is consistent with the observed genetic changes found in all known SARS-CoV-2 isolates. • Some SARS-CoV-2 genomic evidence indicates a close relationship with pangolin coronaviruses[165]; data suggests that pangolins may be a natural host for beta-coronaviruses [99-100]. Additional research is needed. • Additionally, "[…] SARS-CoV-2 is not derived from any previously used virus backbone," reducing the likelihood of laboratory origination,[9] and "[…] genomic evidence does not support the idea that SARS-CoV-2 is a laboratory construct, [though] it is currently impossible to prove or disprove the other theories of its origin."[9]	**Current evidence suggests that SARS-CoV-2 accumulates mutations at a similar rate as other coronaviruses. Mutations and deletions in specific portions of the SARS-CoV-2 genome have not been linked to any changes in transmission or disease severity.** • There have been no documented cases of SARS-CoV-2 prior to December 2019 • Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.[10, 19, 124] • The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be 1.04×10^{-3} substitutions per site per year (N = 116 genomes).[74] • Pangolin coronaviruses are closely related to both SARS-CoV-2 and closely related Bat coronaviruses; phylogenetic analysis suggests that SARS-CoV-2 is of bat origin, but is closely related to pangolin coronavirus.[99-100] • The Spike protein of SARS-CoV-2, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV-1.[104] The rest of the genome is more closely related to two separate bat [104] and pangolin[100] coronavirus. • Analysis of SARS-CoV-2 sequences from Singapore has identified a large nucleotide (382 bp) deletion in ORF-8.[143] The effect of this deletion on transmission or virulence is unknown.

SARS-CoV-2 (COVID-19)	PPE – What PPE is effective, and who should be using it?	Forensics – Natural vs intentional use? Tests to be used for attribution.	Genomics – How does the disease agent compare to previous strains?
What do we need to know?	**Most PPE recommendations have not been made on SARS-CoV-2 data, and comparative efficacy of different PPE for different tasks (e.g., intubation) is unknown. Identification of efficacious PPE for healthcare worker is critical due to their high rates of infection.** • What is the importance of aerosol transmission? • What is the effective distance of spread via droplet or aerosol? • How effective are barriers such as N95 respirators or surgical masks? • What is the appropriate PPE for first responders? Airport screeners? • What are proper procedures for reducing spread in medical facilities / transmission rate in medical settings? • How effective are homemade masks at reducing transmission?	**Identifying the intermediate species between bats and humans would aid in reducing potential spillover from a natural source.** • What tests for attribution exist for coronavirus emergence? • What is the identity of the intermediate species? • Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2?	**Research linking genetic changes to differences in phenotype (e.g., transmissibility, virulence, progression in patients) is needed.** • Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human? • Are there different strains or clades of circulating virus? If so, do they differ in virulence?

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
Attack rate	Proportion of "at-risk" individuals who develop infection	Defined in terms of "at-risk" population such as schools or households, defines the proportion of individuals in those populations who become infected after contact with an infectious individual
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	Official name for the virus previously known as 2019-nCoV.
COVID-19	Coronavirus disease 19	Official name for the disease caused by the SARS-CoV-2 virus.
CFR	Case Fatality Rate	Number of deaths divided by confirmed patients
PFU	Plaque forming unit	Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.
$TCID_{50}$	50% Tissue Culture Infectious Dose	The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R_0	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate

CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.
Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.
Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0, and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures

ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells
ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death
PPE	Personal protective equipment	Gowns, masks, gloves, and any other measures used to prevent spread between individuals
PCR	Polymerase chain reaction	PCR (or real-time [RT] or quantitative [Q] PCR) is a method of increasing the amount of genetic material in a sample, which is then used for diagnostic testing to confirm the presence of SARS-CoV-2

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