SARS-CoV-2 (COVID-19)	Infectious dose – how much agent will make a normal 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?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we know?	• The human infectious dose of SARS-CoV-2, which causes coronavirus disease 19 (COVID-19) is currently unknown via all exposure routes. Animal data are used as surrogates. • Rhesus macaques are infected with SARS-CoV-2 via the ocular conjunctival and intratracheal route at a dose of 700,000 PFU (10^6 $TCID_{50}$).[51] • A total dose of 700,000 plaque-forming units (PFU) of SARS-CoV-2 infected cynomolgus macaques via a combination intranasal and intratracheal exposure (10^6 $TCID_{50}$ total dose).[109] Macaques did not exhibit clinical symptoms, but shed virus through the nose and throat.[109] • Nonhuman primate infection may not represent human infection. • 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 polymerase chain reaction (PCR) primers used in the study do not align well with SARS-CoV-2, casting doubt on this study.[14] • The infectious dose for SARS in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).[49-50] • Genetically modified mice exposed intranasally to doses of MERS virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.[7, 41, 81, 150]	• Pandemic COVID-19 has caused 214,894 infections and 8,732 deaths[72] in at least 173 countries and territories (as of 3/18/2020).[27, 114, 135] • There are 7,769 SARS-CoV-2 cases across 50 US states, with 118 deaths. (as of 3/18/2020)[72]; there is sustained community transmission of COVID-19 in the US.[17] • High-quality estimates of human transmissibility (R_0) range from 2.2 to 3.1[93, 98, 106, 142, 149] Early estimates of the attack rate in China range from 3%-10%, mainly in households.[137] • SARS-CoV-2 is believed to spread through close contact and droplet transmission,[31] with fomite transmission[73], i.e., germs left on surfaces, and close-contact aerosol transmission also plausible.[22] • 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.[138] • Pre-symptomatic[151] or asymptomatic[12] patients can transmit SARS-CoV-2; between 12%[54] and 23% [90] of infections may be caused by asymptomatic or pre-symptomatic transmission. • SARS-CoV-2 is present in infected patient saliva,[124] lower respiratory sputum,[131] and feces. [86] • Social distancing and behavioral changes are estimated to have reduced COVID-19 spread by 44% in Hong Kong,[47] and a combination of non-pharmaceutical interventions (e.g., school closures, isolation) are likely required to limit transmission.[59] • Up to 86% of early COVID-19 cases in China were undiagnosed, and these infections were the source for 79% of documented cases.[84]	• Early genomic analysis indicates similarity to SARS,[154] with a suggested bat origin.[5,42, 154] • Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[108] The identity of the intermediate host remains unknown.[85, 87-88] • Positive samples from the South China Seafood Market strongly suggests a wildlife source,[33] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.[18, 43, 144, 148] • Experiments suggest that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS,[141] potentially explaining its high transmissibility; the same work suggests that differences between SARS-CoV-2 and SARS-CoV Spike proteins may limit the therapeutic ability of SARS antibody treatments.[141] • Modeling between SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.[129] • There is currently no experimental evidence that SARS-CoV-2 infects domestic animals or livestock, though it is expected that some animal species could be infected.	• 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.[79] Fewer than 2.5% of infected individuals show symptoms sooner than 2 days after exposure.[79] • The reported range of incubation periods is wide, with high-end estimates of 24,[60] 11.3,[11] and 18 days.[83] • Individuals can test positive for COVID-19 despite lacking clinical symptoms.[12, 35, 60, 120, 151] • Individuals can be infectious while asymptomatic,[31, 110, 120, 151] and asymptomatic individuals can have similar amounts of virus in their nose and throat as symptomatic individuals.[155] • Infectious period is unknown, but possibly up to 10-14 days [5, 84, 114] • On average, there are approximately 4[54] to 7.5[83] days between symptom onset in successive cases of a single transmission chain. • Most individuals are admitted to the hospital within 8-14 days of symptom onset.[153] • Patients are positive for COVID-19 via PCR for 8-37 days after symptom onset.[153] • Individuals may test positive via PCR for 5-13 days after symptom recovery and hospital discharge.[77] The ability of these individuals to infect others is unknown. • According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.[78] • Experimentally infected macaques were not capable of being reinfected after their primary infection resolved.[13]

SARS-CoV-2 (COVID-19)	**Infectious dose – how much agent will make a normal 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?**	**Incubation period – how long after infection do symptoms appear? Are people infectious during this time?**
What do we need to know?	• Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route	• Capability of SARS-CoV-2 to be transmitted by contact with fomites (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?[71] • Can individuals become re-infected with SARS-CoV-2? • What is the difference in transmissibility among countries? • Is the R0 estimate higher in healthcare or long-term care facilities?	• 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)?	• 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?
Who is doing experiments/has capabilities in this area?	*Capable of performing work* - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Christian Althaus (Bern) - Neil Ferguson (MRC) - Gabriel Leung, Joseph Wu (University of Hong Kong) - Sara Del Valle (Los Alamos) - Maimuna Majumder (Boston Children's Hospital) - Trevor Bedford (Fred Hutchinson Cancer Center) - Sang Woo Park (Princeton)	*Capable of performing work:* - Vincent Munster (Rocky Mountain National Laboratory) - Matthew Frieman (University of Maryland Baltimore) - Ralph Baric (University of North Carolina) - Stanley Perlman (University of Iowa) - Susan Baker (Loyola University Chicago) - Mark Denison (Vanderbilt University) - Vineet Menachery (University of Texas Medical Branch) - Jason McLellan, Daniel Wrapp, Nianshuang Wang (University of Texas) - David O'Conner (U. Wisconsin, Madison)	*Performing work:* - Chaolin Huang (Jin Yin-tan Hospital, Wuhan, China) - The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

SARS-CoV-2 (COVID-19)	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?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we know?	• The majority of COVID-19 cases are mild (81%, N = 44,000 cases)[120] • Initial COVID-19 symptoms include fever (87.9% overall, but only 43.8% present with fever initially[60]), cough (67.7%[60]), fatigue, shortness of breath, headache, reduction in lymphocyte count.[32, 38, 68] Headache[37] and diarrhea are uncommon[68, 82] • Complications include acute respiratory distress (ARDS observed in 17-29% of hospitalized patients,[40, 67] which leads to death in 4-15% of cases[40, 68, 130]), pneumonia,[96] cardiac injury, secondary infection, kidney failure, arrhythmia, sepsis, and shock.[60,68,130, 153] • Approximately 15% of hospitalized patients were classified as severe,[60, 120] and approximately 5% of patients were admitted to the ICU.[60, 120] • Most deaths are caused by respiratory failure or respiratory failure combined with myocardial (heart) damage.[111] • The case fatality rate (CFR) depends on comorbidities; cardiovascular disease, hypertension, diabetes, and respiratory conditions all increase the CFR.[120, 153] • The CFR increases with age; individuals older than 60 are at higher risk of death,[120, 153] and >60% of confirmed fatalities have been male.[120] • Children of all ages are susceptible to COVID-19,[53] though generally present with milder symptoms.[39] Severe symptoms in children, however, are possible.[89] • In the US, 34% of hospitalizations have been individuals less than 44 years old.[4] Based on one patient, a productive immune response is generated and sustained for at least 7 days.[121]	• PCR protocols and primers have been widely shared among international researchers[26, 45, 83, 116, 132, 136] though PCR-based diagnostic assays do not differentiate between active and inactive virus. • A combination of pharyngeal (throat) RT-PCR and chest tomography are the most effective diagnostic criteria (correctly diagnosing 91.9% of infections).[104] Single throat swabs alone detect 78.2% of true infections, while duplicate tests identify 86.2% of infections.[104] • Nasal and pharyngeal swabs may be less effective as diagnostic specimens than sputum and bronchoalveolar lavage fluid.[131] • RT-PCR tests are able to identify asymptomatic cases; SARS-CoV-2 infection was identified in 2/114 individuals previously cleared by clinical assessment.[66] • The FDA released an Emergency Use Authorization enabling laboratories to develop and use tests in-house for patient diagnosis.[58] • Updated tests from the US CDC are available to states.[26, 31] • US CDC has expanded patient testing criteria to include symptomatic patients at clinician discretion.[16] • Several rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,[48] BGI,[19] and Cepheid.[128] • The US CDC is developing serological tests to determine what proportion of the population has been exposed to SARS-CoV-2.[74] • Machine learning tools are being developed to predict severe and fatal COVID-19 cases based on CT scans.[117]	• Treatment for COVID-19 is primarily supportive care, including mechanical ventilation and antibiotics to prevent secondary infection as appropriate.[60] • Preliminary reports from two clinical trials in China suggest that favipiravir improves lung function and reduces recovery time in COVID-19 patients.[126] • Early results suggest that tocilizumab may be effective at treating severe COVID-19 cases.[145] • Press reports of a small clinical trial suggest that chloroquine is effective at reducing symptom duration.[1] • Combination lopinavir and ritonavir with standard care was no more effective than standard care alone.[24] • Corticosteroids are commonly given to COVID-19 patients[153] at risk of ARDS,[146] but their use is not recommended by the US CDC.[29] • Multiple entities are working to produce a SARS-CoV-2 vaccine,[8] including NIH/NIAID,[63, 80] Moderna Therapeutics and Gilead Sciences,[2-3, 94] and Sanofi with HHS.[21] Moderna has begun phase 1 clinical vaccine trials in humans in WA state.[107] • Regeneron Pharmaceuticals has developed potential SARS-CoV-2 antibody therapies.[99] • The development of a coronavirus fusion inhibitor in the lab suggests efficacy across multiple human coronaviruses.[143] • Takeda Pharma (Japan) is working to create antibody treatments based on infected patient plasma.[62]	*SARS-CoV-2 Data* • SARS-CoV-2 can persist on plastic and stainless steel surfaces for up to 3 days (at 21-23°C, 40% RH), with a half-life of 13-16 hours.[125] • SARS-CoV-2 has an aerosol half-life of 2.7 hours (particles <5 µm, tested at 21-23°C and 65% RH).[125] *Surrogate Coronavirus data*: • Studies suggest that other coronaviruses can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)[25, 36], and porous surfaces for up to 3-5 days (SARS-CoV)[56] in air conditioned environments (20-25°C, 40-50% RH) • Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[25, 36, 102, 127] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[127] • SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.[25] • Beta-coronaviruses (e.g., SARS-CoV) may be more stable than alpha-coronaviruses (HCoV-229E).[102] • No strong evidence for reduction in transmission with seasonal increase in temperature and humidity.[92] • One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)[100] • The aerosol survival of related human coronavirus (229E) was relatively high, (half-life of ~67 hours at 20°C and 50% RH), indicating ~20% of infectious virus remained after 6 days.[70] Both higher and lower RH reduced HCoV-229E survival; lower temperatures improved survival.[70]

SARS-CoV-2 (COVID-19)	**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?**	**Medical treatment – are there effective treatments? Vaccines?**	**Environmental stability – how long does the agent live in the environment?**
What do we need to know?	• How long does it take for infected individuals to recover outside of a healthcare setting? • Is the reduction in CFR through time an indication of better treatment, less overcrowding, or both?	• False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual	• Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?[115] • Is the GLS-5000 MERS vaccine[147] cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS[46, 119] and MERS[34] • 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?[15]	• 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.)
Who is doing experiments/has capabilities in this area?	- Jin Yin-tan Hospital, Wuhan, China - China-Japan Friendship Hospital, Beijing, China - Peking Union Medical College, Beijing, China - Capital Medical University, Beijing, China - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China - Huazhong University of Science and Technology, Wuhan, China - The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China - Tsinghua University School of Medicine, Beijing, China - Zhongnan Hospital of Wuhan University, Wuhan, China - Peking University First Hospital, Beijing, China - Peking University People's Hospital, Beijing, China - Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China - The Fifth Medical Center of PLA General Hospital, Beijing, China	*Performing work:* - CDC - Wuhan Institute of Virology - Public Health Agency of Canada - Doherty Institute of Australia - Cepheid - BGI - Fudan University	*Performing work:* - Peter Doherty Institute for Infection and Immunity - Academy of Military Medical Sciences, Beijing, China - Tim Sheahan (University of North Carolina) - Takeda Pharma. (Japan) - Regeneron Pharmaceuticals - CureVac (Germany) *Capable of performing work:* - Ralph Baric (University of North Carolina) - Matthew Frieman (University of Maryland Baltimore) - Sanofi, with BARDA - Janssen Pharma and BARDA[64] *Funded work:* CEPI ($24 million to seven groups): NIAID/NIH: - Moderna and Kaiser Permanente for mRNA vaccine Phase I trial.[3] - University of Nebraska Medical Center Trial (multiple therapeutics including Gilead's Remdesivir).[2]	*Capable of performing work*: - Mark Sobsey (University of North Carolina) - DHS National Biodefense Analysis and Countermeasures Center (NBACC) - Defence Science and Technology Laboratory (Dstl) - Public Health Agency of Canada - CDC - EPA - NIH