COVID-19 What We Know

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Abstract

Human coronavirus diseases are a large family of viruses that occur worldwide and cause a variety of respiratory illnesses from the common cold to more severe diseases that can adversely affect young children, older adults, persons with comorbid health conditions, persons who are immune compromised, and persons living in low-socioeconomic environments. Coronaviruses are known to spread from person-to-person, between people who are in close contact with one another (less than 6 feet apart), through respiratory droplets, and touching contaminated items or inanimate surfaces. Measures to prevent exposure or contamination require proper hand-washing, use of personal protective equipment, social distancing of 6-feet apart, covering mouth and nose when coughing or sneezing and proper disposal of tissues, and properly cleaning frequently used surfaces with approved cleaning and disinfecting solutions. Efforts are underway to curb the spread and to eradicate SARS-CoV-2 through several experimental pathways that include antiviral therapy, vaccine trials, use of convalescent plasma, and monoclonal antibody therapy. This article addresses what is known about SARS-CoV-2 and what is not known, but what is needed to know to stop the spread of this virulent disease.

Keywords: Coronaviruses; COVID-19; Experimental trials; SARS-CoV-2

Introduction

There are seven human coronaviruses identified: (1) HCoV-229E, (2) HCoV-NL63, (3) HCoV-OC43, (4) HCoV-HKU1, (5) Middle East Respiratory Syndrome (MERS-CoV), (6) Severe Acute Respiratory Syndrome (SARS-CoV-1), and (7) COVID-19 (SARS-CoV-2) [1-3]. Human coronavirus diseases occur worldwide (endemic and pandemic), refer to a large family of viruses known to be zoonotic (transmitted from animals to humans), and cause a variety of respiratory illnesses from the common cold to more severe diseases such as MERS-CoV, SARS-CoV and SARS-Co [4-7]. The coronaviruses are major positive-stranded ribonucleic acid (RNA) viruses from the Corona viridae family [8,9]. Corona viruses are named for their appearance in the electron microscope, which shows their surfaces with elliptic virions or projections of corona (crown-like spikes) from the Latin word for crown [2,10,11].

Taxonomy

The seven human coronaviruses, there are two alpha and five beta coronaviruses. There are seven human coronaviruses, two alpha and five beta coronaviruses. The two alpha coronaviruses are HCoV-229E, discovered in the 1960s and HCoV-NL63, discovered in 2004 in Holland isolated from an infant admitted for respiratory distress. The five beta coronaviruses are HCoV-OC43, discovered in the 1960s, SARS-CoV-1 in 2003, HCoV-HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 in 2019 [1-4,7].

The World Health Organization (WHO) issued the interim name for the latest human coronavirus, 2019-nCoV on February 11, 2020, because it originated in the year 2019, the “n” indicating novel, the “CoV” referring to coronavirus, and categorized the virus under SARS-CoV-2 [1,10]. This action was taken to avoid inappropriate use of newly discovered diseases and cultural insensitivity to national, regional, ethnic, or professional groups, and was also endorsed by WHO’s partnering agencies which included the World Organization for Animal Health (OIE) and Food and Agriculture Organization (FAO) [12,13]. The International Classification of Diseases (ICD) final name for SARS-CoV-2 is decided upon by the International Committee on Taxonomy of Viruses [4,14].

Epidemiology

SARS-CoV-2 was first reported as an outbreak in Wuhan, China in December 2019 [4,8,15,16]. As of 2021, according to the John Hopkins Coronavirus Resource Center [17], there are over 84.3 million COVID cases worldwide, with approximately 20.4 million cases in the U.S. and more than 350,000 COVID-19 deaths in America (John Hopkins, 2021) and 507,188 global deaths, and in the United States (U.S.), there were 121,4 thousand deaths and 2.6 million confirmed cases as of June 29, 2020 [1]. Researchers have shown that SARS-CoV-2 spreads from close human to human contact, touching contaminated surfaces indirectly by hands and articles freshly soiled by discharges of nose and throat of an infected person), inhalation of air-borne droplets, and self-inoculation of eyes, nose or mouth [18-20].

However, both alpha and beta human coronavirus infections are frequently associated with Upper Respiratory Tract Infections (URTI), but they can also cause inflammation of lung parenchyma leading to Lower Respiratory Tract Infections (LRTIs) such as viral pneumonia or bronchitis (fever, cough, rhinorrhea, headache, chills, malaise, and sore throat), but can advance to acute exacerbations of chronic obstructive pulmonary disease (COPD) [2,7,21]. Coronavirus virions gain entry into human cells by attaching to the host cell through

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an interaction with the "S" protein and its receptor binding site. Some coronaviruses binding site may be located on the "N" terminus of the S1 region of the virus, while others may be located on the "C" terminus of the S1 protein region. In addition, it is unknown why many coronaviruses may also use peptidase as a receptor site to infect the human host [2,11,18]. According to [11], "many α-coronaviruses utilize Amino Peptidase N (APN) as their receptor, SARS-CoV and HCoV-NL63 use Angiotensin-Converting Enzyme 2 (ACE2) as their receptor."

The incubation period for SARS-CoV-2 in the U.S. is estimated from 2 to 14 days, with an average incubation of 5.2 days; while China’s National Health Commission (NHC) estimated a 10 to 14-day incubation period for SARS-CoV-2 [22,23]. Reports out of Italy showed that the most prevalent clinical signs and symptoms of confirmed patients with SARS-CoV-2 included fever (77%-98%), cough (46%-82%), myalgia or fatigue (11%-52%), and shortness of breath (3%-31%) [24]. A literature search conducted by [16], using several databases, found that the most prevalent clinical symptoms include fever (86%-97%), cough (59%-76%), fatigue (34%-68%), dyspnea (21%-40%) and the most co-morbid conditions found included hypertension (14%-22%), diabetes (6%-11%), cardiovascular diseases (4%-7%) and respiratory diseases (1%-3%). The current list of symptoms reported by the [22] include fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, and less frequently, headache, new loss of taste or smell sore throat, congestion or runny nose, nausea or vomiting, and diarrhea [3,22]. Persons presenting with difficulty breathing, chest pain, new onset of confusion, difficulty staying awake, circumoral pallor or cyanosis should seek emergency medical attention immediately [8,5,21,22]. In addition, asymptomatic persons and those who have been exposed to SARS-CoV-2 should take their temperatures, limit physical contact with others and self-quarantine for 14-days, and obtain laboratory testing to confirm the presence of SARS-CoV-2 [8,22].

Protective Measures

Most importantly, individuals experiencing any coronavirus disease should practice general prevention measures to include adequate rest and sleep, eating a well-balanced diet, washing hands frequently with a hand sanitizer (60% alcohol minimum) or soap and water for 20-seconds or longer, dry hands thoroughly with a clean towel or air dry, avoid touching eyes, nose, or mouth with unwashed hands or after touching surfaces, covering mouth with a tissue or sleeve when sneezing or coughing, using a protective face covering, calling the primary care provider before visiting the office, and notify health authorities to assist with contact tracing [22]. The foregoing requirements are essential for people of color who are disproportionately affected by SARS-CoV-2 because the virus is increasing at alarming rates due to underlying health and economic disparities [25]. Data from the COVID-19 tracking project traces racial and ethnic data from reporting states across America and show that people of color account for 24% of SARS-CoV-2 deaths and represents only 13% of the U.S. population [26].

Contact tracing plays a significant role in identifying positive cases, interrupting viral transmission and helps to prevent further spread of the virus. Contact tracing involves four-steps: (1) Case investigation of close contacts, (2) Contact tracing of exposed individuals, (3) Contact support through education, information and exposure reduction, and (4) Self-quarantining by staying at home and maintaining social distancing of at least 6-feet for the 14-days [22]. Face coverings should be worn when in contact with family members during the quarantine period and when outside or in close contact with other people. Asking everyone to wear masks has helped to reduce the spread of SARS-CoV-2 by persons who may be unaware that they have the virus [17,22]. The N95 and KN95 masks are both rated to capture 95%-99% of particles. The KN95 masks are made in China and require wearers to pass a fit test. The N95 masks produced by the 3M Company have stronger breathability standards. However, both the KN95 and the N95 mass filtration efficiency capture salt particles and a tested flow rate of 85L/minute. Surgical masks provide approximately 63% filtration and cotton handkerchiefs provide about 28% filtration [23,27]. It has been reported that “several 3M masks were able to capture over 99% of tiny 0.01-micron particles (10 times smaller than the coronavirus), even while on people’s face” [23,27].

Transmission

Another important finding addresses the persistence of coronavirus on inanimate surfaces. According to [20], coronaviruses can persist on inanimate surfaces such as plastic, metal, aluminum, paper, glass, steel, wood and surgical gloves for up to nine-days. Following a review of 22-studies on human and animal coronaviruses, researchers found that human coronaviruses (SARS-CoV, MERCoV, and SARS-CoV-2) persisted on plastic for 5-days, aluminum 2-8 hours, paper 4-5 days, glass 4-days, steel 48-hours, wood 4 days, and surgical gloves for 8-hours. The literature review also showed that certain biocidal agents were able to effectively inactivate the viruses by disinfecting the surfaces.

The researchers found that by disinfecting surfaces with 62%-71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within one-minute of contact inactivated coronaviruses. However, benzalkonium chloride or 0.02% chlorhexidine digluconate were less effective on deactivating the viruses [20].

Diagnostic Tests

Coronavirus testing continues to be a focal point in healthcare in the identification, timely interventions, and treatment of the disease. To understand the types of tests currently used to identify positive SARS-CoV-2, there must be a discussion on the virus’ genetic makeup.

Coronaviruses are positive-stranded RNA viruses with genomes ranging in size from 27-33 Kilobases (kb). Genomes represent the amount of DNA found in a haploid or single set of unpaired chromosomes. The genomes are important because they encode for “all the enzymes required for viral RNA replication” that infects humans and (2) 3’ structural proteins involved in several viral processes, viral particle formation, and include Nucleocapsid (N), Membrane (M), Envelope (E), and Spike (S) Proteins [22].

Coronavirus testing may include both laboratory and radiographic findings. SARS-CoV-2 have been detected in nasopharyngeal and oral pharyngeal secretion obtained through nasal or throat swabs, URT and LRT specimens, bronchoalveolar lavage fluid and to a lesser extent in stools [3,5]. Under the federal Emergency Use Authorization (EUA) issued by the FDA, coronavirus testing may involve several methods. Currently, tests are conducted using (1) Molecular (Real-
time Reverse Transcriptase (RT) Polymerase Chain Reaction (PCR) assays or isothermal nucleic acid amplification) testing, (2) Viral (antigen) nasopharyngeal or oropharyngeal swabs or saliva that looks for active viral infection and provides results within minutes to hours, and (3) Serologic immune assays that looks for the host antibody (IgM and IgG) that provides evidence of a prior infection with the virus.

Nucleic acid amplification tests are made available through real-time RT PCR test kits that look for the presence of viral genetic material, are highly specific for SARS-CoV-2, and may contain three assays (ingredients), each targeting a different gene in the virus to lessen the chances for mutations [22]. For example, some test kits may target the S-gene, Orf1 gene (human RNA polymerase protein), N-gene, and the E-gene. The nasal / oral swabs or saliva test is used to detect an active viral infection. The specimen collection involves the use of swabs with synthetic fibers and plastic shafts, instead of wooden shafts with materials that may interfere with test results [22]. Once the specimen is collected, swabs are placed in a 2-3 mL viral transport media. The immunosays are serologic tests performed on blood samples from infected persons to detect antibodies specific to the virus.

Each test has significance. PCR testing may not reveal the presence of the virus, if an individual’s intact immune system was successful in removing the virus and its history of invasion, leading to a false negative Sars-CoV-2 test. However, the immunoglobulin serologic test can detect specific antibodies (IgM/IgG) to the virus years after exposure, if missed by the PCR test. Also, the viral antigen or IgM/IgG can be measured quantitively or semi-quantitatively through an automated fluorescent immunoassay system, targeting analyte concentration if the nasal or oral swab yields a false negative [22,28].

Unfortunately, false positives and false negatives continue to limit tests accuracy [3,15,28]. On March 16, 2020 the FDA announced guidance on types of testing and suggested that “antibody serology tests should not be used as the sole basis for diagnosis of SARS-CoV-2” because it may limit the effectiveness of the test [28], greater concern is that the FDA is unaware of a validated antibody test available for diagnosis of SARS-CoV-2 infection [28]. Radiographic results from coronaviruses tend to show unilateral and bilateral infiltrates, multiple areas of consolidation, pleural effusions, and ground glass opacities [2,8,24].

Management

To-date, there is no cure for coronaviruses. However, social distancing of 6-feet, washing hands after touching surfaces, avoiding self-inoculation, and wearing face coverings have shown to decrease the spread of SARS-CoV-2 [29,30]. Healthcare workers who properly use Personal Protective Equipment (PPE) during patient care also decrease risk of exposure to SARS-CoV-2 [8]. Persons with mild symptoms may not require hospitalization. If symptoms worsen with progression to the LRT, patients may require in-hospital care and the use of Remdesivir or Tocilizumab, an immune modulator [5,8,24,31]. In hospital treatment is supportive, as well as aggressive, and geared towards protecting against multi-organ failure. Patients are provided with oxygen support using nasal canula, Noninvasive Mechanical Ventilation (NMV), Invasive Mechanical Ventilation (IMV), using nasal canula, Noninvasive Mechanical Ventilation (NMV), and Extracorporeal Membrane Oxygenation (ECMO) [5,24].

Antimicrobial agents are used to treat LRT infections, although bronchodilators and systemic corticosteroids are given if indicated [2,5]. Other diagnostic tests that may be elevated include complete blood count which tends to show leukopenia or leukocytosis, end-organ related indices such as Aspartate Serum Transaminase (AST), Lactate Dehydrogenase (LDH), elevated C-reactive protein serum ferritin due to inflammation, and coagulation related indices such as D-dimer and prothrombin time [5,15]. Vaccine development has received support nationally and internationally to stop the spread of COVID-19 and lead in the efforts to create herd immunity.

SARS-CoV-2 Experimental Treatments

To-date, there is no cure for coronaviruses, although multiple treatments are in experimental stages and include convalescent plasma, monoclonal antibodies, antiviral drugs such as Veklury (Remdesivir), and vaccines. Convalescent plasma comes from donors who have recovered from COVID-19 and usually contains antibodies to SARS-CoV-2 [32]. Regenron’s COVID-19 Outpatient Trial using monoclonal antibodies involved 524 patients and has been shown to reduce viral load, patient visits and hospital stay, as well as progression of COVID-19. In the past 30-days, two vaccine manufacturers, Pfizer-BioNTech and Moderna, received FDA emergency use authorization. Both vaccines are synthetic nucleic acids that use fragments of mRNA technology to produce an adaptive immune response [28].

According to Biegel, data showed that Remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. Persons with mild symptoms may not require hospitalization. If symptoms worsen with progression to the LRT, patients may then require in-hospital care and the use of Remdesivir or Tocilizumab, an immune modulator [5,8,24,31]. In hospital treatment is supportive, as well as aggressive, and geared towards protecting against multi-organ failure. Patients are provided with oxygen support using nasal canula, Noninvasive Mechanical Ventilation (NMV), Invasive Mechanical Ventilation (IMV), or IMV with extracorporeal membrane oxygenation (ECMO) [5,15]. Antimicrobial agents are used to treat LRT infections, although bronchodilators and systemic corticosteroids are given if indicated [2,5].

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Vaccine Trials

Currently, there are several vaccine trials underway in America. The list includes: Can Sino Biologics (CanSinoBio), Inovio, Sinovac, Novavax, Gamaleya research, CureVac, Clover Biopharmaceuticals, Merck & Co, Johnson and Johnson, and Sanofi/GlaxoSmithKline (Sanofi/GSK). Prior to the EUA approval, both Pfizer-BioNTech and Moderna reported a 94% efficacy rate [33,34].
Phase 3 clinical trials are designed to determine if an investigational drug (vaccine) can prevent the targeted disease and how long will the protection last. Today, the investigation seeks to evaluate if the new vaccine can prevent COVID-19 in adults. Phase 3 trials require large and diverse population group volunteers to participate who have not been exposed to COVID-19. However, recruitment of these needed population groups is slow in obtaining volunteers, in part due to mistrust of government, dating back to the Tuskegee Syphilis Study, to a slow release of phase 1 and phase 2 trial results.

The goal of the U.S. government is to have a vaccine ready for general use by the end of the year or early next year. The speed of COVID-19 vaccine production is unparalleled and never has a vaccine been developed so quickly following FDA guidelines on safety, efficacy, production and distribution. There are many unanswered questions. Pfizer-BioNTech and Moderna require a two-dose regimen at a 28 and 21 day interval [33,34]. The question for healthcare providers is how do you increase the adherence or return visits of persons receiving their first COVID-19 vaccine dose for dose number two? What are the known adverse effects of the vaccines outside of muscle soreness following the injection? Will there be one or two required injections from all manufacturers or have studies shown that a one-dose vaccine can adequately boost the immune system to respond, if an exposure occurs? Who will be responsible for the cost of the vaccine? Will healthcare workers/healthcare providers be financially protected by the federal Counter Measures Injury Compensation Program (CICP), which is a federal relief program created to cover monetary cost of medical and other expenses to persons seriously injured by use of certain countermeasures during a public health emergency, if adverse effects occur? Are there established healthcare centers or hospitals affiliated with the vaccine programs that are located in high risk areas (hot spots)? What strategies are in place to motivate individuals to take the vaccine? Will there be a rank order on who receives the vaccine first, equitable distribution?

Answers to the many of the questions listed above are being addressed by members of Operation WARP Speed and the Department of Health and Human Services (HHS), and is now being provided to the general public. Currently, HHS activities are directed towards developing a national tracking system among the States, linking provider enrollment authorization to track vaccine orders and delivery. The logistics are unclear on obtaining patient data across different jurisdictions. Nonetheless, according to Paul Mango, Deputy Chief of Staff for Policy in the office of the Secretary at HHS, the goal is to deliver approximately 60 million vaccine doses by the end of 2020. Unfortunately, as of January 4, 2021, over 13 million COVID-19 vaccines have been distributed in America, but less than 4.3 million people have received the vaccine [35]. Other logistical challenges include transporting the vaccines in ultra-cold storage units versus using dry ice; creating injection kits composed of needles and syringes; developing an automatic reminder service that would be inclusive of transient populations such as homeless persons.

Vaccines

The goal of vaccines is to boost the immune system of the human body to identify and eliminate foreign substances from the body through a complex system of interacting cells located within the immune system. The most important action of the immune system is to mount an immune response to an antigen through the production of immunoglobulin’s which are B-lymphocytes protein molecules and cell-mediated T-lymphocytes [36].

Immunity is acquired through two mechanisms, passive and active immunity. Passive immunity provides immediate, but temporary protection against an infection and is produced by an animal or human that is transferred to another human [36,37]. Passive immunity is limited and may last for a few weeks before protection is lost. The earliest example of passive immunity is seen in maternal-infant transfer of Immunoglobulin (Ig) G from the placenta to the infant in the last two-months of pregnancy. IgG provides the infant with temporary protection from certain infections and diseases until the child’s immune system is able to develop its own antibodies [21].

Active immunity is obtained through stimulation of an individual’s immune system by an antigen, production of antibodies and cellular immunity. Active immunity is acquired in two ways: (1) An individual is infected with an antigen, survives the infection, and receives lifelong immunity from the disease, with exceptions such as malaria and influenza [22,36]. Lifelong immunity is achieved by the production of immunologic memory B-cells circulating in the blood and residing in the bone marrow; (2) An individual can receive a vaccine injection containing an antigen that is effective in stimulating antibody production and memory cells without experiencing the disease [22,36].

Vaccines are classified as live, attenuated (weakened) and inactivated with distinct characteristics. Live, attenuated vaccines are derived from “wild” viruses or bacteria that are weakened through laboratory repeated culturing [36]. This process of serial tissue culturing may take up to 10-years to convert a wild virus into an attenuated virus, as seen in the measles vaccine [22].

Live, attenuated vaccines require a small dose of a virus or bacteria to stimulate an immune response, which is usually identical to the immune response produced by the natural infection [22,36]. The body’s immune system does not differentiate between an infection caused by a live, attenuated vaccine from an infection caused by a wild virus or bacteria. However, live, attenuated vaccines are not free of severe or fatal infections, which may occur if there is an uncontrolled replication of the vaccine’s virus or bacteria. If a disease occurs resulting from a live, attenuated vaccine, it is usually mild and is classified as an adverse reaction to the vaccine [22]. Nonetheless, an adverse occurrence usually affects individuals with compromised immune systems as seen in persons with leukemia or Human Immunodeficiency Virus (HIV) infections.

In contrast, inactivated vaccines contain dead viruses, cannot replicate, requires multiple doses to produce immunity, and cannot cause the disease, even in immune compromised individuals [22,36]. The first dose of an inactivated vaccine serves as a primer for the immune system. The second or third doses produce a protective immune response. There is little cellular immunity gained from inactivated vaccines and antibody titers diminish over time. Therefore, some inactivated vaccines will require booster doses periodically to increase or boost antibody titers [22].

Monoclonal Antibodies

According to [32,38 there are several monoclonal antibodies under investigation and in development for both the treatment and
prevention of SARS-CoV and SARS-CoV-2 by neutralizing both viruses from infecting cultured cells.

Monoclonal Antibodies (mAB) have also been used in the treatment of Zika, Ebola and HIV [38]. mAB are “purified antibodies cloned from a single cell” and are engineered to bind to a single specific antigen by neutralizing the antigen [36,38]. mAB are usually produced in Chinese hamster ovary cells; but alternative developments include using plants, algae, and fungi to produce the antibodies [38].

The bulbous projections appearing on the coronavirus are Spike proteins which act as hooks to allow the virus to latch on to and enter the host cell. By binding to a single cell antigen like the Spike protein, mAB neutralizing affect binds distinct epitopes on receptor binding domains on SARS-CoV-2 and synergistically neutralizes the virus. mAB used in blood transfusions consisting of human blood products also provide passive immunity because they are directed at one or more related groups of antigens and usually will not interfere with responses to live vaccines [39].

Conclusion
In conclusion, we know that coronaviruses are respiratory diseases that can cause severe acute respiratory syndrome and is spread primarily through close person-to-person contact or touching objects contaminated with the virus and then self-inoculating by touching eyes, nose, or mouth. To prevent the spread of COVID-19, recommendations include using standard precautions that include proper hand hygiene, initiating contact precautions by wearing gloves, gowns or eye protection, if indicated. Current diagnostic tests provide rapid antigen and serological tests to detect the presence of antibodies in the blood. Experimental treatments include antiviral drugs, uses of convalescent plasma, monoclonal antibodies, and vaccines.

What we do not know and need to know is the degree of antibody protection, individual vulnerability to treatment, associated costs, vaccine safety outside of phase III, and the impact on low income and vulnerable communities with decrease access to health care and healthy foods. Due to increased employment struggles, high stress levels (allostatic loads), and factors surrounding coronaviruses including COVID-19, increase the risk of getting and dying from the disease [24]. Also, additional research is needed in the effects of social distancing and face covering protection. Most importantly, everyone is responsible for helping to stop the spread of this deadly viral disease by taking approved CDC steps to protect themselves and others, and consulting with a primary care physician on receiving the COVID-19 vaccine.

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References
22. Centers for Disease Control and Prevention (2020) Symptoms of coronaviruses. Centers for Disease Control and Prevention, Georgia, USA.


35. Centers for Disease Control and Prevention (CDC).


