COVID-19: Treatment and Prevention
By Mark Fagan

Overview of the Disease

SARS-CoV-2 is the novel coronavirus that causes the disease, COVID-19. Coronaviruses are a large family of viruses that are common in people and many different species of animals. Rarely, animal coronaviruses can infect people and then spread between people such as with MERS-CoV, SARS-CoV, and now with this new virus (named SARS-CoV-2). All three of these viruses have their origins in bats. SARS-CoV-2 was identified in China in late 2019 and resulted in a pandemic with infections in 184 countries. There is no vaccine and it hits the elderly and those with diabetes, respiratory problems, heart problems, and weakened immune systems particularly hard.

This growing pandemic is resulting in millions of cases and hundreds of thousands of deaths worldwide. The Alabama Department of Public Health reported 2,800 cases in Alabama on April 10, 2020. Researchers at Johns Hopkins Coronavirus Resource Center are concerned that the number of reported COVID-19 deaths is underestimating the scale and severity of the pandemic. The challenges with reporting COVID-19 cases include limited testing and a focus on the most severe cases. Many potential COVID-19 patients may be dying without a proper diagnosis or dying at home and not tested after death. Further complicating death counts is that people with underlying conditions might be dying with COVID-19 and not because of it.

The current pandemic has stressed the health care system more than any event since the 1918 Spanish Flu pandemic (675,000 deaths in U.S. out of 103 million population). There were no vaccines and no antibiotics to treat secondary infections, so control efforts were limited to isolation, good personal hygiene, and use of disinfectants. In that pandemic, communities closed schools, churches, bars, and other social venues. While the closures remained, there were lower mortality rates. However, transmission rebounded once controls were lifted.

Pandemics begin with an investigation phase, followed by recognition, initiation, and acceleration phases. The peak of illnesses occurs at the end of the acceleration phase, which is followed by a deceleration phase, during which there is a decrease in illnesses. Different countries can be in different phases of the pandemic at any point in time and different parts of the same country can also be in different phases of a pandemic.

Researchers at the Imperial College of London reported that early studies of those infected with the SARS-CoV-2 virus showed 81% developed loss of taste/smell, cough, fever, and shortness of breath within 2-14 days. In addition to these symptoms, 14% developed mild pneumonia with another 5% ending up with respiratory failure and multiorgan system dysfunction with almost half of those dying. Severe symptoms were developed from 5 to 8 days with ICU admission in 10 to 12 days. Deaths showed 80% were among adults 65 years and older.

According to the U.S. Centers for Disease Control (CDC), one third of transmission occurs in the household, one third in schools and workplaces, and one third in the community. The average infected person spreads the disease to two or three others. Symptomatic individuals are highly infectious, but those without symptoms can also transmit the virus. The World Health Organization (WHO) states that COVID-19 spreads mostly through respiratory droplets. It may be possible that a person can get COVID-19 by touching an object that has the virus on it and then touching their own mouth, nose, or eyes. On recovery from infection, individuals are assumed to be immune to re-infection in the short term.

The COVID-19 pandemic has resulted in the largest medical mobilization in U.S. history. Hospital beds, intensive care beds, ventilators, and personal protective equipment for health care workers (masks, gowns, shields) have been in short supply. Alternate care sites have included retrofitting existing facilities, utilizing gymnasiums or convention centers, or establishing field hospitals using tents. Staffing these facilities will likely remain a challenge. Health care workers are continually being stressed as the deaths increase.

Personal hygiene (hand washing and sanitizing) and masks can help to reduce transmission of SARS-C0V-2. Suppression (home isolation of those infected and their household members for 14 days) and social distancing (six feet apart and no large groups) can reduce the number of cases. The federal government is working closely with state, local, tribal, and territorial partners, as well as public health partners, to respond to this public health threat. Foreign nationals who have been in China, Iran, the United Kingdom, Ireland and any one of the 26 European countries in the Schengen Area within the past 14 days cannot enter the United States. U.S. citizens who have been to those countries within the past 14 days can enter the U.S., but they are subject to health monitoring and possible quarantine for up to 14 days.

COVID-19 Testing

Diagnostic tests are a key part during any disease outbreak. They identify infected people for isolation and can be used for identifying those whom they had contact. The CDC developed a test to diagnose COVID-19 and commercial labs are now producing their own tests. These tests analyze mucus samples for SARS-CoV-2. Rapid blood tests for COVID-19 are developing to determine those who had it and developed antibodies (immunity). Large-scale testing, including people without symptoms, could determine the actual number of cases. Monitoring antibody levels in people who have recovered can help to determine how long immunity lasts.

Treatment for COVID-19

Patients without pneumonia might be able to manage their illness at home. Hospitalization is needed to manage pneumonia, hypoxemic respiratory failure/ARDS, shock, multiorgan failure, secondary infections, thromboembolism, and gastrointestinal bleeding. Hydroxychloroquine (HCQ) (approved in 1955 for treating malaria, lupus, and rheumatoid arthritis) and azithromycin (antibiotic) have been used off label to treat COVID-19 with many anecdotal reports of success. The Food and Drug Administration (FDA) is conducting trials on the effectiveness of these drugs for treating COVID-19. HCQ's prevention qualities for COVID-19 are also under examination (there are some correlations from insurance records that show people already taking HCQ are not coming down with COVID-19). HCQ could quickly be available in large quantities.

The National Institutes of Health (NIH) began a randomized controlled trial for the treatment of COVID-19 patients with the antiviral drug remdesivir (used to treat Ebola). The WHO announced a study, which could include thousands of patients in dozens of countries, for the use of the following drugs to treat COVID-19: remdesivir, HCQ, lopinavir and ritonavir (two HIV drugs), and interferon-beta. INSERM, the French biomedical research agency, is coordinating an add-on trial in Europe that will include 3,200 patients from at least seven countries.

Convalescent plasma from those recovered from COVID-19 is being tested as a treatment (one at the Mayo Clinic). Plasma from recovered patients has been used previously to treat other diseases. Convalescent plasma can be used now though the Compassionate Use exception.

A biotech company in San Francisco (Distributed Bio) has developed a promising treatment for COVID-19 using plasma from SARS patients (mutating antibodies from SARS). The next steps involve tests by the military of this treatment on live coronavirus and then accelerated human

trials possibly this summer. The company suggests that this antibody treatment could be ready by September and approved for Compassionate Use by the FDA and could serve as a short-term vaccine for three to six months.

Vaccines for COVID-19

SARS in 2002 and MERS in 2012 (caused by two other coronaviruses) did not produce long-term immunity, so reinfection with these viruses could occur after 10 months. Vaccines are the only way to develop long-term immunity. A vaccine is given to artificially stimulate the immune system and hopefully not make people sick. When the body comes in contact with the real disease, it is able to fight it off. Scientists have sequenced the genome of SARS-CoV-2 and there are more than 40 companies claiming candidate vaccines. If one or more of these vaccines proves safe and effective in animal models, they could be ready for larger-scale human trials as early as June.

Clinical trials usually take place in three phases. The first involves a few dozen healthy volunteers testing the vaccine for safety and monitoring for adverse effects. The second, involving several hundred people, looks at how effective the vaccine is, and the third does the same in several thousand people. Screening out duds is essential, which is why clinical trials are not skipped or hurried.

The Center for Biologics Evaluation and Research (CBER) regulates vaccines in the USA. Once a vaccine is approved, billions of doses could be needed for world distribution. Many companies in the COVID-19 vaccine race might not have the necessary production capacity or financing. Production facilities tend to be tailored to specific vaccines and scaling up for unproven vaccines might not be commercially feasible. Which vaccine candidates are the most likely to succeed have to be determined. Estimates are that it will take 12 to 18 months to develop a proven vaccine and then longer to produce it, distribute it, and put it to use.

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