

Coronavirus: A Moving Target for Medical and Vaccine Research

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The coronavirus pandemic has spread to nearly all countries, resulting in tens of millions of infections and hundreds of thousands of deaths. Dozens of companies have been working on vaccines, hoping to curb the disease.

Recent discoveries, however, indicate that from its genetic mutations to its route of spread, and from its symptoms to its damage to the immune system, coronavirus is anything but a normal disease and poses significant challenge to vaccine research.

Nearly 200 Genetic Mutations

The coronavirus disease is a respiratory illness, but its targets are beyond the lungs. “[The disease] can attack almost anything in the body with devastating consequences,” says cardiologist Harlan Krumholz of Yale University in an April article in *Science* titled “How does

coronavirus kill? Clinicians trace a ferocious rampage through the body, from brain to toes.”

Scientists at the Los Alamos National Laboratory published a draft paper titled “Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2” at BioRx (www.biorxiv.org) on May 5, 2020, announcing 14 mutations of coronavirus they had identified associated with the surface protein called spikes. One of the mutations, D614G, has been found to be more transmissible than regular coronavirus strains.

The finalized paper was later published in Cell on July 3, 2020, with the title “Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus.” The paper found that the D614 mutation has been the most prevalent form in the global pandemic, as observed on the national, regional, and municipal levels.

Further analysis indicated that this variant grows rapidly in the lab while infected individuals also have a higher viral loads in the upper respiratory tract.

Another paper, titled “Emergence of genomic diversity and recurrent mutations in SARS-CoV-2,” is to be published in Infection, Genetics and Evolution in September 2020 by

scientists from University College London. By analyzing over 7,600 public genome assemblies, the authors identified 198 recurrent mutations. While all these mutations shared a common ancestor at the end of 2019, they occurred in different regions of the genome, including non-structural proteins and spike proteins.

And the situation keeps changing. “Chinese doctors are seeing the coronavirus manifest differently among patients in its new cluster of cases in the northeast region compared to the original outbreak in Wuhan, suggesting that the pathogen may be changing in unknown ways and complicating efforts to stamp it out,” reported Bloomberg on May 20, 2020, in an article titled “China’s New Outbreak Shows Signs the Virus Could Be Changing.”

More specifically, the virus mutants seem to have a longer incubation time for developing symptoms and appear to be more persistent afterwards.

Unusual Symptoms

The typical coronavirus symptoms include cough, fever, muscle aches, headaches, and difficulty in breathing. But there are also unusual symptoms such as skin rashes, diarrhea, kidney abnormalities, and risky blood blots,

something rarely seen for respiratory viruses, reported Time magazine in an article titled “Unusual Symptoms of Coronavirus: What We Know So Far” on May 19, 2020.

Scientific American published an article titled “From Headaches to ‘COVID Toes,’ Coronavirus Symptoms Are a Bizarre Mix” on May 18, 2020, speculating there are two main mechanisms that lead to problems in almost every organ, including the brain, heart, kidneys, gastrointestinal tract, and skin. One of the mechanisms involves one’s immune response, and the other is blood clotting.

Clotting-related complications such as lung artery blockage and stroke were seen in as many as 30% of critically ill patients. What puzzles scientists is that it could happen even to middle-aged people and in unusual places in one's body.

“Genetic sequencing showed some patients have gene variants associated with a hyperactive immune response to viral infections, yielding one possible clue into why some people develop serious complications,” according to doctors at Columbia University Irving Medical Center, as reported by the Wall Street Journal on May 7 in an article titled “Coronavirus Hijacks the Body From Head to Toe, Perplexing Doctors.”

Other scientist agree. "It comes across more as a systemic disease exhibited initially as a respiratory disease," says Mark Poznansky, director of the Vaccine & Immunotherapy Center at Massachusetts General Hospital, in a May article on Axios titled "The coronavirus is a moving target." For example, it is unclear whether the cause is the virus itself, the immune system's response to it, or the treatment received, explained the article.

Devastating Effect on the Immune System

Normally, a person infected with a pathogen could develop antibodies that would fend off pathogen were it to attack the individual again. But for coronavirus, only around 10% to 15% of the infected population have developed immunity, said Danny Altmann, an immunologist from London to CNBC on July 6. "Its a very deceitful virus, and immunity to it is very confusing and rather short-lived," he explained.

Additional research, on the other hand, has shown that a low amount of antibodies could instead aid the entry of the virus into cells, making it more deadly to the body. This phenomenon is referred to as antibody-dependent enhancement, or immune enhancement. It has been

observed for Yellow fever virus, Zika virus, HIV, and now coronavirus.

This situation has been confirmed by vaccine developers, reported Nature on June 5 in an article titled “Coronavirus vaccine developers wary of errant antibodies.” More specifically, “vaccines generating antibodies against SARS-CoV-2 may bind to the virus without neutralizing it. Should this happen, the non-neutralizing antibodies could enhance viral entry into cells and viral replication and end up worsening infection instead of offering protection,” the article wrote.

In addition to immune enhancement, other factors also contribute to the damage. COVID-19 results in pneumonia in most cases and acute respiratory distress syndrome (ARDS) in about 15% of the cases, wrote an article in Frontiers in Immunology on June 16 titled “The COVID-19 Cytokine Storm; What We Know So Far.”

“Mortality in COVID-19 patients has been linked to the presence of the so-called ‘cytokine storm’ induced by the virus. Excessive production of proinflammatory cytokines leads to ARDS aggravation and widespread tissue damage resulting in multi-organ failure and death,” the article explained.

A Challenge for Vaccine Research

Producing a vaccine for COVID-19 is not simple. One reason is that coronavirus is a RNA virus, which has a much higher mutation rate compared to DNA viruses.

An example is the flu virus. In the past few decades, flu vaccines have been provided to the public, but the disease still claims about 50,000 lives each year in the United States alone. “The most commonly used flu shots protect no more than 60% of people who receive them; some years, effectiveness plunges to as low as 10%,” wrote an article in the Science magazine in September 2017 with a title of “Why flu vaccines so often fail.”

Between the 1940s and the 1960s, people believed the vaccine had an efficacy of 70%-90% based on antibody levels. Through more accurate methods, such as polymerase chain reaction (PCR), the number of infections in vaccinated populations was found to be much higher.

Several factors contributed to the failure of vaccines, explained Arnold Monto, an epidemiologist at the University of Michigan School of Public Health. One was the mutation of the circulating strain, or “escape mutants”;

the other is mutation of the vaccine strain itself during production.

Vaccine research for coronavirus also has other challenges. Anti-spike antibodies (S-IgG) that bind spike protein on the virus surface have been shown to cause acute lung injury (ALI) by disrupting the immune system, as mentioned above. In a paper published in JCI Insight in February 2019 titled “Anti–spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection,” scientists found similar inflammatory responses also existed in patients who died of coronavirus. Numerous pieces of evidence indicate that COVID-19 can infect more efficiently and replicate more robustly than SARS-CoV.

A Diseases with Many Uncertainties

There are still many unknowns about the coronavirus. The 1918 influenza pandemic was by far the deadliest infectious disease in human history with a death toll of 50 million or more, wrote an April article in the New England Journal of Medicine with a title of “Escaping Pandora’s Box—Another Novel Coronavirus.”

The article wrote that diseases such as pandemics are closely related to human behavior and that such diseases

could accelerate suddenly. “Evidence suggests that wherever it began, it silently spread around the world, causing mostly mild cases but also mortality of 0.5 to 1% or higher—a rate that was initially too low to be detected against a high background rate of death from unrelated respiratory illnesses,” the article wrote. “Then it suddenly exploded in urban centers almost everywhere at once, making a dramatic entrance after a long, stealthy approach.” Unfortunately, COVID-19 resembles the 1918 influenza pandemic in many ways, including its rapid growth and geographic spread.

What will happen next remains unknown. Altmann from Imperial College London said he expects a second wave and that the situation remains “very, very scary.” He emphasized that it is difficult to predict if or when an effective vaccine for COVID-19 might be identified. “The devil is in the details, vaccines aren’t that easy,” he added.

The Chinese Communist Party (CCP) covered up the 2003 SARS outbreak, and it did the same when COVID-19 broke out. Many patterns have indicated that areas heavily influenced by the CCP have high numbers of cases. With this in mind, rejecting the totalitarian regime of the CCP and returning to traditional values will lead us to a path of safety.

<http://en.minghui.org/html/articles/2020/8/17/186388.html>