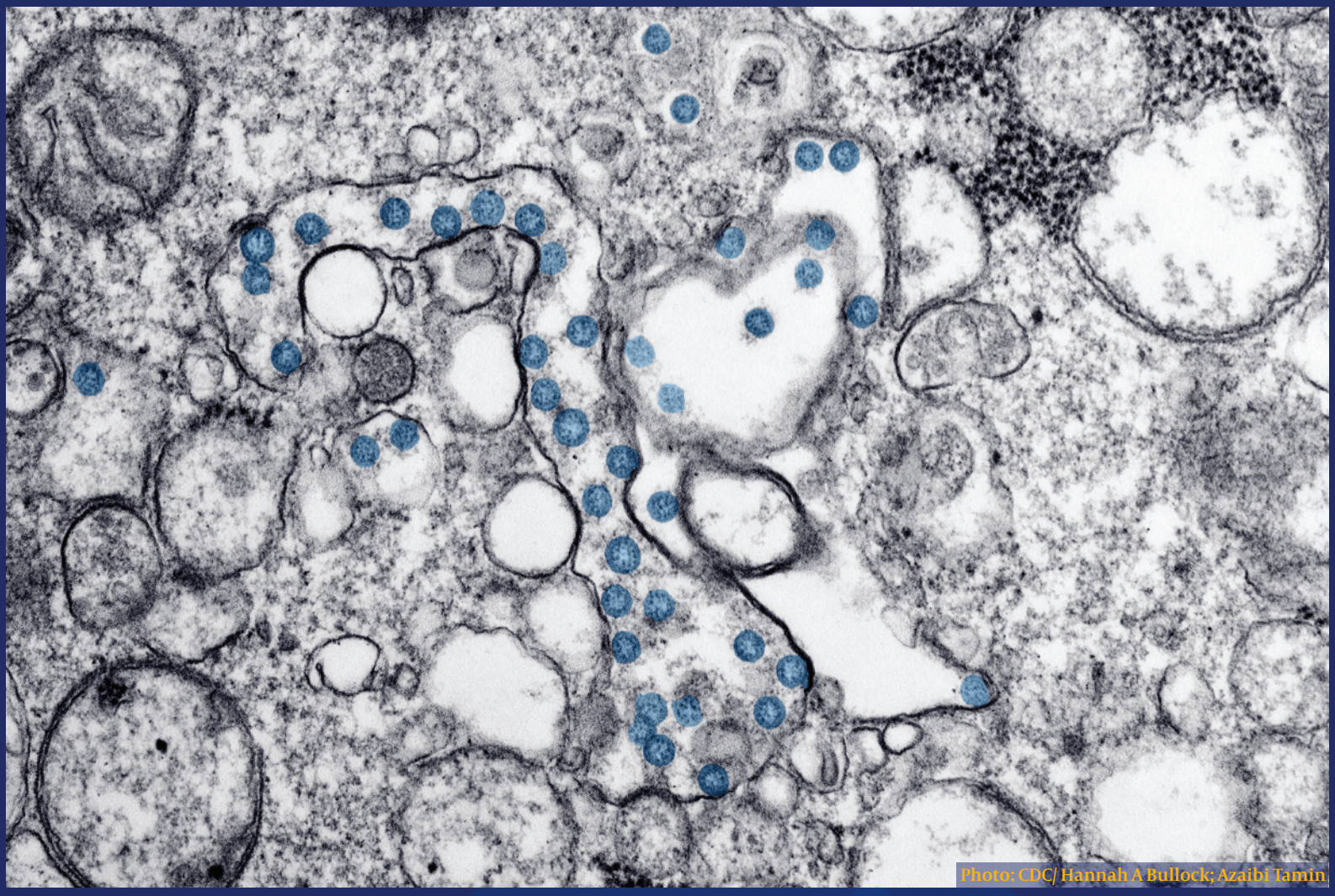

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POSTDOCTORAL SCIENCE WRITERS

COVID-19 Edition Vol. 3 Issue 1; Spring 2021

EMORY UNIVERSITY

About

The Emory Postdoctoral Science Writers Magazine is a bi-annual publication. It is written and edited by postdocs for everyone. The goal of our magazine is two-fold: 1) to highlight research being done here at Emory University as well as in collaboration with other Atlanta area research institutions, and 2) to provide an avenue for those in the postdoc community to be practiced in the art of science writing for a general audience. We in the Science Writers Committee hope you are inspired by these pieces and welcome contributions and editorial services for future issues.

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Cover Image

"Transmission electron microscopic image of an isolate from the first U.S. case of COVID-19, formerly known as 2019-nCoV. The spherical viral particles, colorized blue, contain cross-sections through the viral genome, seen as black dots."

Image ID#23354 contributed by the CDC/ Hannah A. Bullock, and Azaibi Tamin on cdc.gov and available in the public domain, 2020.

A Message from the Chair

About a year ago, the World Health Organization declared COVID-19 a global pandemic. Since then, the viral outbreak has significantly transformed our lives and our world. It is a dreadful crisis that has left so many heartbroken over lost family members. It has been agonizing to sufferers of healthcare disparity and has imposed unprecedented challenges to people's livelihoods. While we grieved for the past, we also reflected for opportunities to renew and learn.

As we march into 2021, we have gained a deeper understanding of the lethal virus and developed vaccines to combat it. These advancements cannot be achieved without the effort of our healthcare workers, medical researchers and scientists in all fields. Since the outbreak of COVID, the Emory community has been taking a lead role in understanding, treating and protecting against the virus. As postdocs at Emory, we are proud to be part of this effort and are highly motivated to stay engaged in this process. This edition of the Emory University Science Writers magazine presents phenomenal digests about the scientific and societal aspects of COVID-19. We hope that this edition offers energy and optimism to the Emory community as we get through this crisis together!

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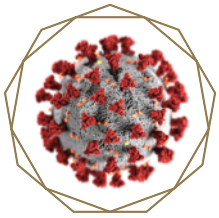

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We thank the Emory Communications and Marketing department for the use of Emory logos and design elements.
We also thank Lydia Soleil, PhD of the Emory OPE for her outstanding guidance and assistance with this publication.

COVID-19 Image ID#23312 from cdc.gov (CDC/ Alissa Eckert, MSMI and Dan Higgins, MAMS)

Extent of Physical Maladies Arising From COVID-19 and Consequent Treatment Methods

The critical health risks associated with COVID-19 are not limited to viral infection, as current treatment methods can be detrimental to physical health with lasting damage.

Jacob Misch, PhD & Skyler Canute, MS

The ongoing pandemic is a topic of great concern. There are widespread reports and accounts of the respiratory ailments, ranging in symptom severity from asymptomatic to critical, which are directly related to the initial wave of the illness. The lesser-known aspect of the coronavirus disease (COVID-19) infection is the myriad of other potential avenues of destruction that can be inflicted on the human body, as well as the unfortunate and brutal impacts of the treatment methods. In some cases, these can be more extreme and long-lasting than the respiratory illness, especially when the potential side effects include damage to the nervous and musculoskeletal systems. From the perspective of physical therapy and rehabilitation engineering, it has become paramount to identify these negative indirect COVID-19 symptoms and mitigate their impacts on recovering patients.

COVID-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2). The shape of the virus features numerous surface proteins that form a halo or corona around its spherical body. When introduced to the environment of the human respiratory system, these surface proteins allow the virus to interface with Angiotensin-Converting Enzyme 2 (ACE2) proteins, which reside on the surfaces of many types of cells within the human body. Typically, these ACE2 proteins act as a defense mechanism against angiotensin II (ANG II) proteins, which are known to increase blood pressure and inflammation and can lead to generalized tissue damage. As such, the body is designed to have ACE2 proteins located throughout the respiratory system (nasal passages, lungs) and among cells in the arteries and veins of every organ to prevent damaging levels of ANG II inflammation. Unfortunately, this means those sites are prime targets for the coronavirus infection. When the SARS-CoV-2 surface proteins bind to the ACE2 receptors, a transmembrane protease TMPRRS2 allows the virus to access and utilize the cells inherent replicative abilities. No method is currently capable of preventing this ACE2-hijacking approach from occurring, and studies have not found any consistent link between the number of ACE2 receptors and susceptibility or severity of COVID-19. In theory a higher density of ACE2 receptors would increase available replication sites, however, reducing the density could lead to increased inflammation due to a lack of ANG II breakdown.

Due to the prominence of ACE2 receptors and TMPRRS2 in the respiratory tract, the mucus-lined membranes and the tissue of the lungs are critical battlegrounds for the body's autoimmune response against the viral infection. If the body can fend off the infection at the upper levels (nose, throat), then the symptoms will likely mirror "common cold" symptoms. In most cases, this is exactly what happens: clinical manifestations of the infection have been fever (89% of cases), cough (58%), and labored breathing (46%). If the virus is makes it to the lower respiratory tract (trachea and lungs), it can cause inflammation and Acute Respiratory Distress Syndrome (ARDS) which can quickly stiffen the lung tissue and fill the area with fluid. Signs of pneumonia can frequently be detected (73%) though only a relatively small percentage of cases (20%) escalate to the point of intensive care, and an even smaller portion (6%) are deemed 'critical'. In critical populations, SARS-CoV-2 causes an intense systemic inflammation which can damage tissue, apply pressure to sensitive areas of the body, weaken the muscles, and flood the central nervous system with cytokines that can lead to severe neuroinflammation.

Neurological manifestations of COVID-19 are reported frequently in the form of dysgeusia (change/loss of taste) and anosmia (change/loss of smell). These can be short-term, where the transmission of the odor to the nerve is simply obstructed by congestion. However, there are many cases of longer-term loss of sensation when the severe inflammatory response to the virus accidentally kills off the olfactory neurons that typically transmit these signals. Neuronal recovery through regrowth is a slow process. This inflammation is not present in just the nasal cavity. Any tissues with dense quantities or ACE2 receptors are at a high risk of neuronal damage, even with medical intervention. The combinatorial effects of immobility during treatment and inflammatory immune response take a significant toll on the musculoskeletal system, especially joints. Myalgia, or

weakness and soreness, was present in anywhere from 30% to 50% of the symptomatic population and these issues had a chance to persist. In one study of severe SARS cases, patients had a steep 32% reduction in grip strength up to 3 months after leaving intensive care, compared to age-matched healthy controls. Furthermore, large concentrations of the SARS-COV-1 virus had spread through mechanoreceptors and gained access to the brainstem, which is the primary interface between the brain and the body for involuntary actions such as maintaining steady heartbeat and breathing. Fortunately, COVID-19 has not been reported traveling through the mechanorecptors to the brainstem yet.

Treating COVID-19 is not trivial due to the ubiquity of the potential viral infection. Pharmaceutical interventions are drastic and, consequently, potentially damaging to the 'healthy' biological mechanisms. For example, chloroquine and hydroxychloroquine are antiviral interventions that are intended to block the fusion of viruses with lysosomes in the cell body (the 'escape route' of the virus from the infected cell). They also have the potential adverse effect of weakening the muscles (myopathy) and neuromuscular behavior (neuromyopathy). Existing muscle pains (myalgia) from the generalized inflammation and the onset of muscle weakness would further inhibit the patient from moving around for the duration of the treatment period. This can start a cyclic pattern where further intervention leads to more pain and inactivity, which only feeds the cycle. Similar cyclic interactions can be observed with the application of other medications. Ribavirin can cause arthralgia and general musculoskeletal pain in up to 10% of cases and, in combination with Interferon α and β, can worsen the symptoms of seemingly unrelated conditions like sarcoidosis. Understanding these side-effects help us differentiate between the symptoms of the virus and the symptoms of the treatment. However, the limited clinical data for more recent treatment methods, such as remdesivir, can be increasingly worrisome as its long-term effects have not been thoroughly assessed.

Physical stress during intervention in severe cases of COVID-19 can be detrimental to the health of the patient overall during treatment, as well as introduce long-term complications during and after the recovery period. The sedentary state of patients during treatment can reduce muscle mass and, in concert with the general inflammation in both organs and muscles, may lead to circulatory issues such as blood clots (thrombosis). Clotting blocks the flow of blood to muscles and organs of the body (ischemia), and can lead to lethal complications if the clots become lodged in the heart or brain where they can cause heart attacks and strokes. The most drastic physical intervention, mechanical ventilation, introduces an entirely different layer of complications to the post-COVID recovery. Short-term (acute) complications such as injury to the upper airways and pneumonia or sinusitis may complicate the treatment period but are unlikely to have any lasting negative impact on the patient. Long-term (chronic) complications, however, pose the threat of month- or year-long recovery times. In addition, weaning patients off ventilation can be a tricky ordeal and is not always successful, especially if their respiratory system has experienced significant damage. Injuries to the trachea from the physical insertion or removal of the ventilator are likely to be painful and long-lasting. This can impair the act of swallowing food and can ultimately lead to malnutrition and dysfunction of gastrointestinal motility. Finally, the patient is susceptible to decubitus ulcers (bedsores) if they are not carefully attended to, which can lead to further infection and complications to the circulatory and lymphatic systems.

COVID-19 will coexist with humans for the foreseeable future, and we need to not only look at getting through the initial symptoms, but also the longer aftereffects. Full inoculation could take years, even without the likely risk of new strains emerging that circumvent existing vaccination attempts. To survive this pandemic and return to 'normal', we must recognize the threats to our health that this virus poses, both as a direct result from viral infection as well as the side-effects of pharmacological and mechanical interventions.

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A Silent Symptom: Anxiety as a Consequence of COVID-19

Stress and COVID-19 infection are associated with the development of anxiety and adverse mental health symptoms during the COVID-19 pandemic.

Jessica Pierce, PhD

The declaration of the novel coronavirus (e.g., SARS-CoV-2 or COVID-19) disease outbreak as an international public health emergency in early 2020 marked the beginning of a tumultuous journey. Fast-paced modern life, distinguished by social gatherings and in-person meetings, became a daily cycle of balancing new work strategies, tuning into constant news coverage, and coping with an aversion to both doorknobs and passers-by. Although change is inevitable, COVID-19 has presented us with abrupt challenges to normalcy that have consequences extending beyond the physical recovery from infection. In particular, the onset of mental health disorders, such as anxiety, have worsened the impact of the COVID-19 pandemic on the population, and the extent of long-term detrimental effects are still being determined.

Many circumstances have contributed to the increased emotional distress associated with navigating life in the COVID-19 pandemic. With uncertainties regarding disease transmission forecasts and stay-at-home orders, millions of people responded to the news of the COVID-19 pandemic by flocking to supermarkets to obtain resources—leading to supply hoarding and the reduced availability of necessary resources. Essential workers were faced with the difficult decision to place themselves at risk in order to ensure the health, safety, and comfort of those around them. Traditional professional and learning environments quickly transformed into virtual worlds, with the boundaries between work and rest fading each day. Further, aside from a looming fear of severe COVID-19 infection, millions of people were burdened with threats of job, housing and food insecurity, social stigma associated with disease transmission, isolation from others, and the loss of loved ones. While any one of these stressors may contribute to the development of anxiety disorders and other psychiatric symptoms, the reality is that most of us are navigating the COVID-19 pandemic within various intersections of these triggers—thus, increasing the risk for adverse psychosocial effects. An assessment of mental health, substance abuse, and suicidal ideation in U.S. adults conducted by the CDC COVID-19 Response Team in June 2020 showed an increased prevalence of adverse mental health conditions as compared to data reported in the second quarter of 2019. By late June 2020, 40.9% of the participants reported at least one adverse condition, including anxiety or depressive disorder (30.9%), trauma- or stressor-related disorder symptoms (26.3%), increased substance use to cope with stress or emotions related to the pandemic (13.3%), or suicidal ideations during the 30 days preceding the survey (10.7%). The incidence of at least one of these symptoms increased to more than half of respondents in groups that included adults 18-44 years of age (with the highest rates in young adults aged 18-24 years; 74.9%), Hispanic participants, essential workers, and unpaid caregivers for adults. A separate assessment of healthcare employees in New York further demonstrated the strain of the COVID-19 pandemic, with over 50% of surveyed frontline workers reporting psychological distress due to concerns of transmitting COVID-19 to their families, lack of control in their personal or clinical work environments, patient deaths, and limited availability of PPE, among other issues. Additional screenings showed that large proportions of the healthcare workers exhibited adverse mental health conditions such as acute stress (57% positive on a PC-PTSD scale), depression (48%; PHQ-2), and anxiety (33%; GAD-2)—with nurses exhibiting significantly higher rates of psychological symptoms than physicians and house staff across parameters ($p \leq 0.004$). These data highlight the alarming incidence of adverse mental health conditions associated with the threat of COVID-19 and the unexpected lifestyle changes that ensued.

Recent work has also indicated that COVID-19 infection may be directly associated with negative psychiatric symptoms. Clinical screening of some COVID-19 survivors one month after hospital treatment indicated that 42% of patients self-rated in the pathological range for anxiety (as determined by STAI-state ≥ 40 scores in the IES-R self-report questionnaire at first clinical contact), with 59% of the patients who scored positive for clinical anxiety reporting no previous psychiatric history of anxiety disorders prior to

COVID-19 infection. Other psychiatric conditions, such as post-traumatic stress disorder, obsessive-compulsive symptoms, and insomnia were also reported in many COVID-19 survivors, with particularly high rates in patients with a previous history of psychiatric diagnosis. While extensive demographic and lifestyle information was not provided in this study, it is important to consider the potential impact of factors such as social stigma, isolation, an inability to work, and healthcare costs on the mental health prognosis of COVID-19 patients. Interestingly, there was a mild positive association of baseline systemic immune-inflammation index (SII) measurements with anxiety and depression following disease remission, though there are currently limited reports on these relationships in the context of COVID-19. There is an established relationship between emotional distress and physical manifestations, such that exposure to stressful and traumatic events dysregulates the neurobiological processes that control systemic inflammation, behavioral patterns, and the function of various tissues throughout the body. Physiologic responses to acute stressors in anxiety-based disorders are characterized by increased circulating pro-inflammatory cytokines (including TNF, IL-1, and IL-6) that modulate immune responses via mechanisms that are reciprocally controlled by HPA axis activation and glucocorticoid release. However, chronic stress is implicated in suppressed immune function—which occurs in part through the sensitization of immune cells to elevated stress hormones and an increase in inflammatory cytokines—potentially heightening the risk of infection and poor disease outcomes. Further, the detrimental effects of chronic stress on the immune system are exacerbated with one of the leading risk factors for severe COVID-19 infection—aging. These complex relationships illustrate the potential for multidisciplinary research concerning COVID-19, its psychosocial impact, and inflammatory immune responses to make significant contributions to our greater understanding of adverse mental health comorbidities in physical illness. With this work, we are making progress to enhance the development of novel strategies for effective public health communication, intervention efforts, and mental health services that prioritize marginalized and at-risk groups that have been disproportionately affected during this pandemic.

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Homing in on a Moving Target: SARS-CoV-2 Immunity and Progress in Vaccine Development

Introduction to SARS-Cov-2 structure, immunity and vaccine development.

Gokul Raghunath, PhD

The emergence and the rapid proliferation of the Covid-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has wreaked havoc on the world's public health system and the economy. By March 2021, the pandemic has claimed over 2.6 million lives worldwide, with the United States accounting for about a fifth of the worldwide death count (530,000 and growing). With limited treatment modalities, the world has resorted to social distancing and strict hygiene measures to mitigate the spread of the virus. However, large scale implementation of such measures in an effective fashion has remained challenging. For these reasons, developing an effective vaccine is one of the most pragmatic ways to curb the progression of the pandemic. This article is intended to be a brief and accessible review of the current literature surrounding the structural basis of SARS-CoV-2 infection, the associated immune response, and the different types of vaccination strategies pursued by scientists around the globe.

SARS-CoV-2 structure and function: How does the infection happen?

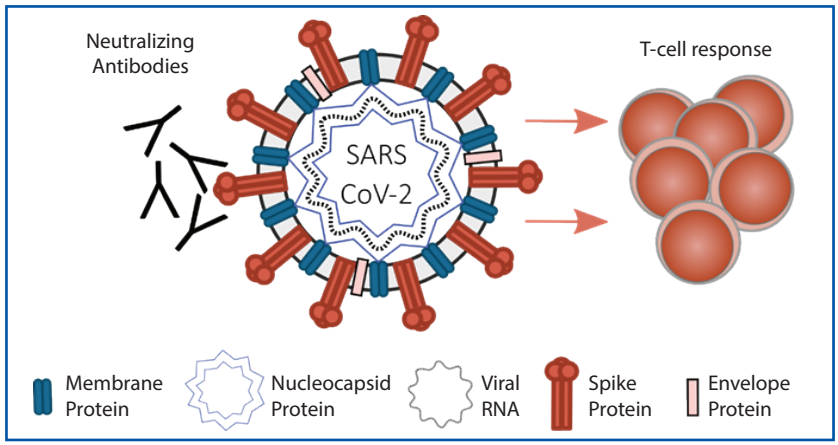
SARS-CoV-2 belongs to the Coronavirus family, a group of enveloped viruses whose genetic material is composed primarily of single-stranded RNA. The genetic material is enveloped by a spherical lipid layer decorated by 3 major structural proteins (see figure): membrane, spike and envelope proteins. Inside the envelope, the viral genome forms a complex with the nucleocapsid proteins, which in turn associate with the membrane proteins.

The infection of the cell is initiated by the interaction of the spike protein with receptors found naturally within (and on) the cell (surface). These receptors are found predominantly on lungs and intestines, and because of this, the cells that line the respiratory system are the primary target of entry for Coronaviruses. After attaching to the receptor proteins, the spike protein undergoes significant structural changes, leading to fusion of the viral and the host-cell membranes. After this process, the viral RNA genome is released into the host cell. The genetic material then hijacks the cell's protein machinery and makes several copies of itself, which are transported out of the cell. The number of viruses within the host multiplies exponentially, with each newly formed virus capable of making multiple copies of itself.

Adaptive immunity: How does the body respond to the infection?

After infection, the body attempts to defend itself against this invading pathogen by activating its immune system. Immunity to SARS-CoV-2 can be achieved either through humoral immunity or through cellular immunity.

Humoral immunity is facilitated by extracellular components (found in body fluids or humors, hence the name) like the antibodies that bind to the viral surface and neutralize the infection. In the case of SARS-CoV-2, the spike protein of the virus is considered the most important target for neutralizing antibodies. The primary role of the neutralizing antibodies is to attach itself to the antigen (spike protein) and facilitate subsequent immune responses. While antibodies can have a protective effect on their own, multiple studies of patients with Covid-19 have shown that antibody levels do not correlate strongly with illness severity. This implies that in addition to humoral immunity, cellular immunity may also play a major role in the defense against Covid-19.



Cellular immunity, as the name suggests, is cell-mediated and does not involve antibodies. Instead, it involves the activation of different types of

cells, such as phagocytes and T-cells, that release chemicals known as cytokines and chemokines in response to the infection. While studies on cellular immunity to SARS-CoV-2 are still ongoing, several small-scale studies have provided us with valuable insights. In some reports, a proportional increase in SARS-CoV-2 specific T-cells relative to other T-cells was observed in the first week post-infection. While this increase was temporary, it was found to correlate well with the severity of the disease. Additionally, a strong correlation between the levels of neutralizing antibodies and number of T-cells targeting the spike protein, hints at the idea that both cellular and humoral immunity work in harmony to address infection.

Vaccine development: The current state of affairs

Development of potent vaccines that leverages the body's immune system to protect against Covid-19 infection has been ongoing for several months. While a comprehensive review of the current approaches is beyond the scope of this article, the various vaccine candidates can be broadly classified as follows: nucleic acid vaccines (i.e. DNA and RNA), live attenuated vaccines, subunit vaccines (i.e. proteins and protein segments), inactivated virus vaccines, and viral vector-based vaccines. Regardless of approach, most of the vaccines developed operate on a common scientific rationale: Inject a small amount of the whole virus (whether attenuated, inactivated, vector based) or individual components of the virus (such as DNA, RNA, or other proteins) and let the body's immune system mount a strong enough response. Once the body has managed to develop a strong immune response, exposure to the real infective virus should not cause serious infection.

Out of the different types of vaccines, mRNA vaccines are perhaps the most intriguing of the lot owing to their nascency. Given that the RNA's innate function is to help convert genetic information stored in DNA to proteins, this type of vaccine leverages the RNA to teach the body's cells to produce a small, harmless portion of the spike protein that acts as the antigen. Because the key component of the vaccine (mRNA) can be produced in-vitro (in a test tube within a lab) at a large scale, mRNA vaccines are simpler, cheaper, and faster to produce than other types of other vaccines. Some of the most popular vaccines that have come into the spotlight recently (e.g. those produced by Pfizer in collaboration with BioNtech and by Moderna in collaboration with the National Institutes of Health) are all mRNA-based vaccines. At the time of writing, Emory University also has a mRNA-based vaccine in Phase 3 clinical trials. During November 2020, Pfizer and Moderna have announced that their vaccines are about 95% efficient in preventing Covid-19 infection in comparison to a placebo. The first official vaccine dose in the US, outside of a clinical trial, was administered to a healthcare professional in New York on 14th December 2020, with millions of doses to be administered through the spring of 2021. Preliminary reports suggest that it is possible to scale the production of mRNA vaccines up to almost 1.3 billion doses by the end of 2021.

Covid-19: the moving target:

Despite the impressive progress made, the first batch of vaccines might not be an "end-all" strategy for Covid-19 elimination. There are several unknown variables that might negatively impact our fight against the disease. First, the safety and longevity of the immunity acquired from vaccines remain unclear. While the manufacturer's press releases claim that the vaccines don't have any side effects; long-term research on these claims have not yet been possible. It is worthwhile noting that there are currently no licensed mRNA vaccines in the United States. This adds an extra level of complexity to vaccine rollout given the difficulty it might pose to establishing public trust. Additionally, several reports have indicated that the immune response to Covid-19 can be short lived. This is a major area of concern, as the possibility of re-infection could make the vaccine ineffective as time goes on. This is further complicated by the fact that many mutations of infective SARS-CoV-2 have already been identified. This implies that a vaccine that is effective against the current strain of the virus might not be as effective in the upcoming months. For all these reasons, it is imperative that the public and scientists continue to stay vigilant and agile during this ongoing fight against the pandemic.

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COVID-19 Infection and Diabetes: A Quick Overview

COVID-19 imposes serious risks to individuals with diabetes.

Becky Yao, PhD

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While most people are concerned about the Coronavirus Disease 2019 (COVID-19), individuals with diabetes may be especially so. The dire challenge posed to the diabetic individuals and the healthcare community around the world has garnered a collaborative effort to effectively prevent and efficiently manage the ongoing pandemic. This article provides a succinct, yet comprehensive overview of the interrelationship between diabetes and COVID-19.

COVID-19 is an infectious disease that can lead to multi-organ functional impairment including the lungs, heart, liver, kidneys, and the brain. It is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which enters the body by binding to a protein that is highly expressed in the cells of many of our main organs. These cells include the most abundant cells in airways of the lungs (lung epithelial cells), muscle cells that constitute the heart (cardiac myocytes), and a layer of cells lining the interface of the vessel wall and flowing blood (vascular endothelium). Diabetic complications account for 17% - 34% of COVID-19 hospitalizations, secondary only to hypertension. In addition, the fatality rate is 2% over all hospitalized COVID-19 patients, but is a staggering 7% for patients with diabetes as well.

Diabetes is a collection of metabolic disorders where either the pancreas produces an inadequate amount of insulin (type 1), a hormone that moves blood sugar into cells, or the body is resistive to insulin (type 2), both affecting the proper storage and use of blood sugar. An estimated 10% of the global adult population is affected by diabetes. Blood sugar is an essential source of energy and nutrients to all cells in the body, including the immune cells. A rapid and effective immune response is crucial for fighting the virus and protecting the body. Individuals with diabetes have weakened immune responses because the immune system is constantly on the alert for the low-grade inflammation arising from the long-standing dysregulated blood sugar. Therefore, these individuals are, in general, more susceptible to infections. In the event of a systemic infection, as in COVID-19, the pre-weakened immune system has no effective approach to combating a viral infection of that magnitude.

Understanding the underlying mechanism of COVID-19 under diabetic conditions is essential for developing therapeutic drugs to treat COVID-19 more effectively among diabetic populations. The link between diabetes and COVID-19 is highly complicated and only partially understood. Studies suggest that the poorly controlled high blood sugar may support viral proliferation, even in individuals with no diabetic history. Evidence indicates that the higher level of inflammatory factors in type 2 diabetes, induced by a high level of blood sugar, may promote significant inflammatory and immune responses in severe COVID-19 patients. These inflammatory factors further contribute to the impaired function of T cells, an important type of immune cell, and to the death of lung epithelial cells, which serve as a defensive layer for the airways.

For either type of diabetes, age is also a key factor. In general, the COVID-19-related mortality odds ratio is 914:1 for those aged 80 and above compared with those under 40 years old, as reported by the National Health Service (NHS) of England in 2020. Unbiased interpretations of reported statistics require a rigorous inspection of the context. When investigating the independent effect of diabetes on the COVID-19 infection, many studies take into consideration the known confounding factors such as demographics, clinical characteristics, and vascular complications. Particularly for type 2 diabetes, whose target population is of advanced age, it is unclear whether aging plays a more central role in the COVID-19 infection among the diabetic population. A study that adjusted for multiple confounding factors, including age, found that both types of diabetes are associated with an increased number of in-hospital COVID-19-related deaths. Nevertheless, identified cases were those critically ill patients or those who registered with clinical practice, excluding individuals with less severe condi-

tions who tend to be younger, and who just recover at home without relying on medical care. What adds to potentially biased interpretations is that diabetes is also a risk factor for some diseases identified as comorbidities of COVID-19. A host of complications associated with diabetes may independently contribute to the severity and mortality of COVID-19. Individuals with type 2 diabetes are at twice the risk of developing heart diseases, and heart diseases are the primary cause of death in type 2 diabetes. The prolonged high blood sugar gradually damages blood vessels that support the transfer of oxygen and nutrients necessary for the normal function of the heart, which leads to heart diseases. The current statistics indicate that the fatality rate of COVID-19 patients with heart diseases is five times greater than those without heart diseases.

Beyond the scope of basic and clinical science in diabetes, the disproportional COVID-19 population is equally complicated. This is because healthcare disparity is often intertwined with race and ethnicity and many socio-economic factors such as low income and poor living conditions. Many studies have reported that the level of education and financial wealth are strong predictors of mortality risk among adult diabetic individuals. These predictors are known contributing factors to poor health outcomes, and are associated with limited access to healthcare services and elevated psychological distress. While healthcare disparity is a long-standing issue, there have been recent pushes to raise public awareness to ensure fair opportunities and resources regarding maintenance and management of people's physical and mental health.

Even though COVID-19 imposes additional challenges on people with diabetes, proactive efforts can be taken for a more preventable or controllable medical outcome. Maintaining a well-controlled blood sugar level is the baseline of diabetes care management. Staying in good mental health is particularly important as well, as increased stress can affect blood sugar levels. In addition, diabetic individuals are highly recommended to engage in physical activities such as ankle rotations and calf massage to enhance blood circulation.

Finally, as our understanding of the connections between diabetes and COVID-19 become deeper, individuals with diabetes will get through this unprecedented time at a more accelerated pace and be relieved from unnecessary struggles.

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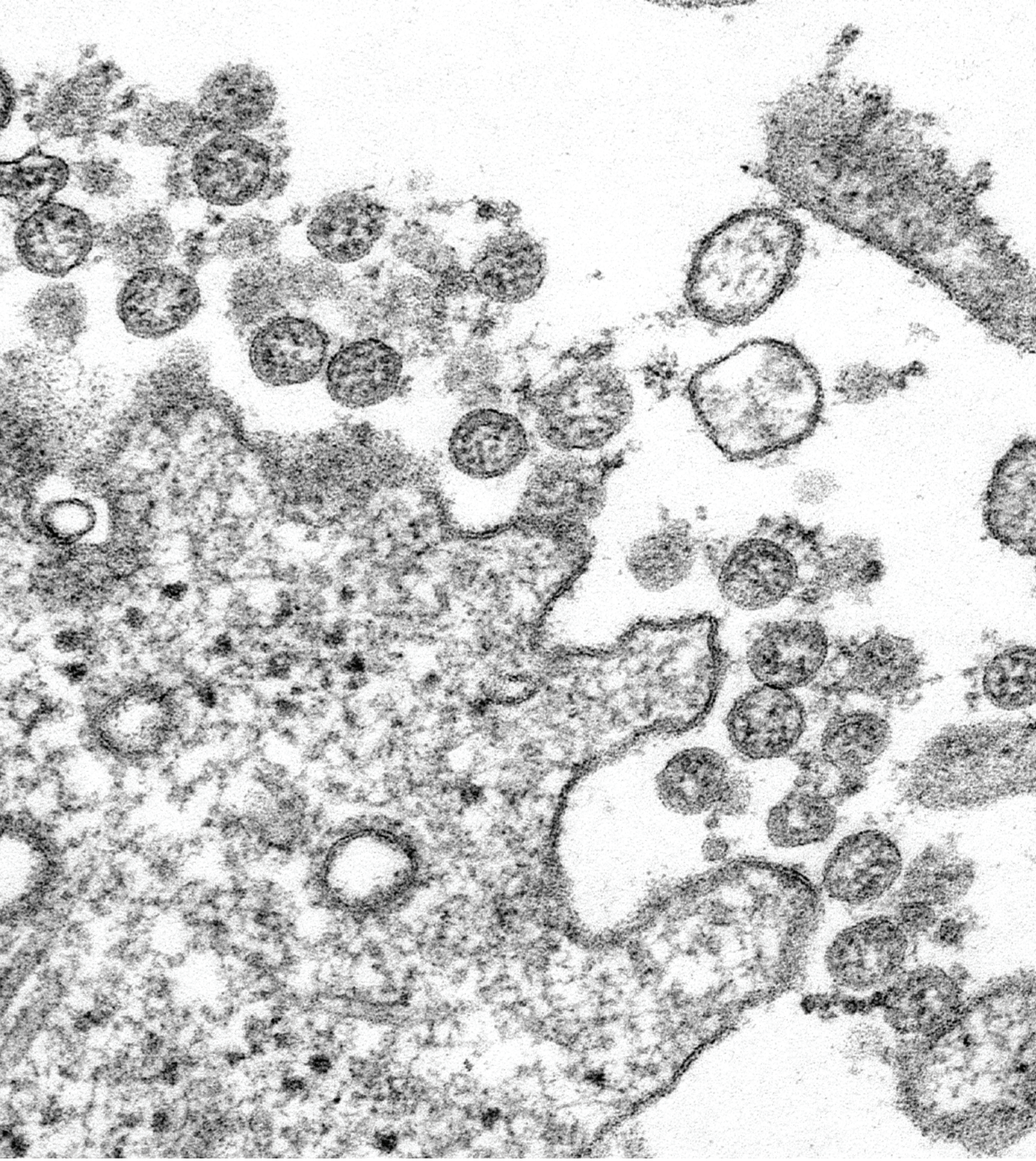

"Transmission electron microscopic image of an isolate from the first U.S. case of COVID-19, formerly known as 2019-nCoV. The spherical extracellular viral particles contain cross-sections through the viral genome, seen as black dots."

Image ID#23336 from cdc.gov (CDC/ Cynthia S. Goldsmith and A. Tamin)