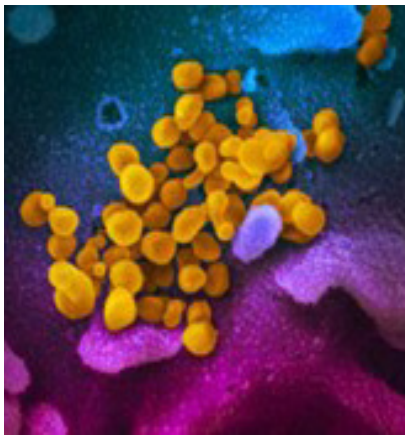
JOHNS HOPKINS MEDICINE

FisherFocus

Summer 2021

NEWS FROM THE SHERRILYN AND KEN FISHER CENTER FOR ENVIRONMENTAL INFECTIOUS DISEASES

Dedicated to the clinical research of environmental pathogens which improves the diagnosis and treatment of these infections.



This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient in the U.S., emerging from the surface of cells (blue/pink) cultured in the lab. **Credit NIAID-RML**

What's Inside

I No Longer Have COVID. Why am I Still Sick?

In the spring of 2020, as people recovered from the first wave of acute SARS-CoV-2 infection responsible for COVID-19, clinicians noted persistent symptoms in up to a third of patients. Although patients no longer demonstrated active infection, they described persisting illness. Dubbed Post-acute Sequelae of SARS-CoV-2 Infection (PASC), "long COVID syndrome," or "long-haul COVID," symptoms can be non-specific across multiple body organ systems. Symptoms may last weeks to months, with most but not all people gradually recovering their health. What is perplexing is the variability in who develops this syndrome. It has been reported in young, previously physically active, healthy adults and those with serious baseline diseases. Curiously, the severity of COVID illness does not predict who will develop PASC.

At this time, there is no agreed-upon definition of what constitutes PASC. However, some authors suggest it be defined as a collection of symptoms developing during or following a confirmed or suspected case of COVID-19 and continue for one month or longer. In addition, there are no diagnostic markers for confirmatory diagnosis of PASC. Therefore, diagnosis is based currently on clinical judgment. Nevertheless, surveys of patients reveal PASC has a significant impact on lives, causing considerable disruption in physical activity, work and personal relationships.

Not Just COVID

For infectious diseases clinicians, prolonged symptoms after a viral or bacterial infection, not just SARS-CoV-2, have been a perplexing problem. Similar lingering symptoms have been reported in approximately 10% of people six months or more after diagnosis with mononucleosis (Epstein-Barr virus), Q fever (Coxiella burnetii bacteria), Ross River valley arthritis (alphavirus) and Lyme disease (Borrelia bacteria). The variable nature of the symptoms makes it very difficult to tease out the mechanisms and if certain people are at heightened risk. Moreover, similarities with Chronic Fatigue Syndrome/myalgic encephalitis may pose similar problems as a heterogeneous condition that has defied explanation for decades. For example, are symptoms related to chronic, undetectable infection or left-over debris of infection, is it hormonally-related, are there abnormalities in the cell powerplants/the mitochondria, or is it immune-related? Are symptoms caused directly by the infection, or does the virus trigger a pre-existing predilection?

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SYMPTOMS OF PASC ("LONG COVID")

Fatigue
Muscle pain or weakness
Joint pain
Brain fog, difficulty thinking
Difficulty concentrating
Anxiety or depression
Lightheadedness, fainting
Headache
Shortness of breath
Chest pain or tightness
Cough
Palpitations
Post-traumatic stress disorder (PTSD)
Rapid heart rate
Intermittent fever
Sleep difficulties

MESSAGE FROM THE DIRECTOR

For more than a decade following the 1918 influenza pandemic, a mysterious Parkinson-like syndrome with sleepiness, less responsive muscles and subsequent high mortality appeared to develop in hundreds of thousands across the globe. Popularly termed encephalitis lethargica, in 1920, the US Surgeon general declared that the epidemic 1918 Spanish influenza was the cause. However, opinions varied, especially as outbreaks of the disorder often differed from respiratory infections thought to represent influenza. More than a century later, questions remain about how this epidemic of neurological disease was transmitted, what caused the syndrome, and are there effective treatments?

Some similar challenges now confront patients and modern medicine with the range of symptoms following the SARS-CoV-2 infection that may persist for weeks or months after acute illness. Clinicians are asked how to help patients complaining of impairing symptoms such as fatigue, shortness of breath, brain fog, musculoskeletal pain, anxiety and low mood. In addition, investigators tackling epidemiology, pathogenesis or interventional strategies face issues that can be especially vexing when complaints are subjective and are otherwise commonplace in the general population.

For example, how to sort out a 34-year-old who had mild COVID-19 two months ago but who now complains of symptoms while also under stress and complaining of burnout due to the pandemic and extended work hours while juggling home life demands? How much is due directly to infection versus factors of work and home life?

While the numbers of coronavirus infection in the United States are diminishing, the aftermath of this terrible pandemic will continue to affect many whether they have post-acute sequelae of SARS-CoV-2 (PASC) or have loss of friends, family or jobs that have upended life. Lessons from the pandemic will hopefully emerge with better preparedness for the next threat that surely will emerge.

Research including by Johns Hopkins investigators now have funding that is orders of magnitude greater than past efforts over the last decades tackling chronic fatigue and post-infectious fatigue syndromes. Among the toughest of puzzles to crack, understanding these problems in the context of COVID-19 hopefully will lead to both diagnostic tests that help validate the diagnosis as well as specific therapeutic approaches to speed recovery.

BreakOut

Vivien Thomas Scholars Initiative

Launched with a recent gift, the Vivien Thomas Scholars Initiative will expand and diversify Johns Hopkins PhD programs in the sciences, technology, engineering, and math. The inaugural director of the new $150 million effort will be Damani Piggott, MD, PhD, a clinician and researcher in the Division of Infectious Diseases and a former receipient of Fisher Center funds for his research on prosthetic joint infections. In addition, Dr. Piggott serves as Assistant Dean for Graduate Biomedical Education and Graduate Student Diversity in the School of Medicine. We congratulate Dr. Piggott on this new program and look forward to future collaboration with the Fisher Center.

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Seeking Solutions

Unfortunately, despite the sizeable number and wide variety of triggers for post-viral syndromes, little research has been conducted, which has not led to breakthroughs. However, the perpetual low funding of fatigue syndromes is due to change. The widespread distribution of PASC and the deserved media attention may be one of the silver linings coming out of the terrible pandemic. In addition, investigations into PASC may lead to discoveries benefiting other perplexing post-viral maladies. How will this be done?

The National Institutes of Health (NIH) has set aside $1.15 billion for the study of PASC. Funds will be used to identify the causes of PASC and develop ways to treat individuals and ultimately prevent the disorder. The first series of Research Opportunity Announcements was issued in February 2021 for the development of data repositories, mobile health platforms, and core resources to support other NIH PASC Initiatives. It is anticipated the knowledge gained will benefit patients beyond PASC. According to Francis S. Collins, MD, PhD, Director of NIH, "We believe that the insight we gain from this research will also enhance our knowledge of the basic biology of how humans recover from infection, and improve our understanding of other chronic post-viral syndromes and autoimmune diseases, as well as other diseases with similar symptoms."

The Fisher Center has supported the efforts of Yukari Manabe, MD and Paul Blair, MD, MPH, to determine the long-term outcomes of COVID-19. The team was one of the first to describe the clinical course and frequency of prolonged symptoms among those with mild COVID-19 not requiring hospitalization. Among 118 outpatients, one-third (34%) were not in their usual state of health four weeks after infection onset. The study continues to follow patients at 6 and 12-month intervals. The team notes challenges with in-person follow-up visits to the campus and has pivoted to telephone and online surveys during the pandemic. Investigators will gather additional data from the Johns Hopkins Precision Medicine Analytics Platform (PMAP), collect data from health systems, and gain robust analysis from larger datasets. By using sophisticated "big data" analytics, additional patterns and insights may be revealed that would be missed if not for machine learning.

Managing PASC

Johns Hopkins has taken steps to understand and manage PASC. The Johns Hopkins Post-Acute COVID-19 Team (JH PACT) service collaborates with Pulmonary & Critical Care Medicine, Physical Medicine and Rehabilitation, and the Johns Hopkins Home Care Group. The service offers comprehensive medical management and rehabilitation services, including physical, occupational and speech-language therapy.

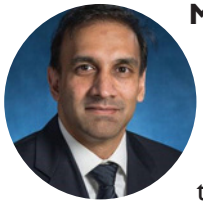
The Johns Hopkins POTS Program is one of the few centers in the US dedicated to understanding and treating Postural Orthostatic Tachycardia Syndrome (POTS) which afflicts a subset of PACS patients. POTS is a dysfunction of the autonomic nervous system, and the ability to regulate blood flow is dysfunctional. With POTS, when changing position from reclining to a sitting or standing position, the person feels lightheaded (or faints), along with decreased blood pressure and a racing heart. Often triggered by a viral infection, not all PASC patients experience POTS. There is an overlap between the symptoms of POTS and those of PASC and chronic fatigue syndrome (myalgic encephalomyelitis). Symptoms may respond to physical therapy, medications and increased salt and water in the diet.

Recognizing that PASC poses significant health challenges that may last beyond the pandemic, the Fisher Center is proud to have contributed to advancing knowledge about this mysterious ailment. Johns Hopkins continues to research and offer care to our post-COVID patients.

More information about PASC may be found at:
https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/covid-long-haulers-long-term-effects-of-covid19

FISHER CENTER DISCOVERY PROGRAM 2021

While the Fisher Center Discovery Program (FCDP) continues to focus on environmental infectious diseases, the Center embraced the challenges to human health raised by the COVID-19 pandemic by permitting consideration of SARS-CoV-2 research for the 2021 grant cycle. Thanks to the continued generosity of Sherrilyn and Ken Fisher, eight FCDP grants were recently awarded.



Maxim Rosario, MBBCh BAO
Assistant Professor in the School of Medicine, Department of Pathology

Using mice infected with the mold Aspergillus, the study will compare treatment using either white blood cells or natural killer cells. If successful, this approach could be trialed in humans with weakened immune systems.

Meghan Davis, DVM, PhD
Associate Professor in the School of Public Health, Department of Environmental Health and Engineering
Amanda McCormick, BS (Doctoral Student)

This study will explore how chronic exposure to the common bacteria Staphylococcus aureus influences the immune system in asthma. The research may aid in identifying markers of susceptibility to other diseases such as SARS-CoV-2.

Netz Arroyo, PhD
Assistant Professor in the School of Medicine, Department of Pharmacology and Molecular Sciences

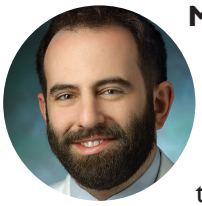
The team will adapt widely available glucometers to measure SARS-CoV-2 antibodies in saliva. If successful, the use of hand-held point-of-care technology, like repurposed glucometers, may be adapted for other pathogens and pandemics.

Maged M. Harraz, MD, PhD
Instructor in the School of Medicine, Department of Neuroscience

The study will create a luminescence assay for high throughput screening of existing compounds that could reduce the severity of SARS-CoV-2 infection. This technique rapidly and efficiently identifies existing compounds that may be useful.

Challice Bonifant, MD, PhD
Assistant Professor in the School of Medicine, Department of Oncology

The research will evaluate cell therapy as a potential novel therapeutic for SARS-CoV-2 infection. This technique replaces dysfunctional cells with healthy cells and may have many applications for other viral diseases or oncologic targets.



Matthew Robinson, MD
Assistant Professor in the School of Medicine, Department of Medicine, Division of Infectious Diseases

The team will develop a suite of web tools to predict progression to severe disease and death in patients with SARS-CoV-2 infection. The developed tools may lead to improved clinical outcomes for patients.

Karen Carroll, MD
Professor in the School of Medicine, Department of Pathology, Division of Medical Microbiology
David Gaston, MD, PhD (Pathology Fellow)

The investigators will use next-generation sequencing (NGS) to find otherwise unidentified pathogens causing lung infections in COVID-19 patients. NGS techniques may be applicable to other diseases, not just lung infections and COVID-19.

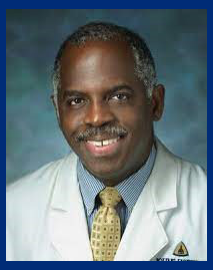
Nitipong "Nate" Permpalung, MD, MPH
Assistant Professor in the School of Medicine, Department of Medicine, Division of Infectious Diseases

The team will use a urine test to aid in COVID-19 associated pulmonary aspergillosis screening and diagnosis. If successful, the test may be used in non-COVID patients, along with the possibility of urine tests for other disease-causing entities.

Managing Deployment of COVID-related Grants

Based on the successful management mechanics demonstrated by the Fisher Center Discovery Fund grants program, Johns Hopkins University leadership tasked Fisher Center staff to solicit and manage review of two grant programs related to COVID-19: research related to SARS-CoV-2 vaccines and research related to post-acute COVID-19 syndrome. In March, 2021 the following six grants were awarded to Johns Hopkins faculty.

COVID-19 VACCINE-RELATED RESEARCH FUND

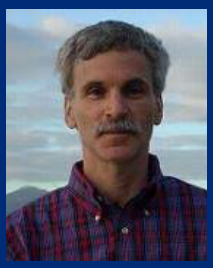


Joel Blankson, MD, PhD
Professor in the School of Medicine, Department of Medicine, Division of Infectious Diseases

The study will compare the effect of SARS-CoV-2 vaccination on people living with HIV and healthy donors, informing vaccine dosing strategies. Results will be relevant to COVID-19 and other vaccines in people living with HIV.

Jacqueline Garonzik Wang, MD, PhD
Associate Professor in the School of Medicine, Department of Surgery, Division of Transplant Surgery

The study will address SARS-CoV-2 vaccine adverse reactions and immune durability in persons with solid organ transplants. Results will be relevant to COVID-19, but also for the use of other vaccines in this population.



Carl Latkin, PhD
Professor in the School of Public Health, Department of Health, Behavior and Society and Department of Epidemiology and in the School of Medicine, Department of Medicine, Division of Infectious Diseases

The research will assess vaccine attitudes and beliefs, while developing messaging strategies to increase vaccine uptake among racial and ethnic minority adults. Results will be translated into toolkits to inform public health vaccine roll-out programs for COVID-19 and other vaccines.

POST-ACUTE COVID-19 SYNDROME DISCOVERY FUND

Nisha Gilotra, MD
Assistant Professor in the School of Medicine, Department of Medicine, Division of Cardiology

The research will assess patients recovering from COVID-19 to determine the prevalence and determinants of myocardial dysfunction. This may lead to improvements in screening and therapy for these patients.

Shenandoah "Dody" Robinson, MD
Professor in the School of Medicine, Department of Neurosurgery

The team will develop serum biomarkers in an attempt to prevent post-acute COVID neurological events. This strategy may be beneficial for other neuroinflammation disorders.

Steven Menez, MD, MHS
Assistant Professor in the School of Medicine, Department of Medicine, Division of Nephrology

The team will evaluate subclinical acute kidney injury in outpatient COVID-19 patients. The goal of this study is to predict which clinical patients will develop progressive kidney disease.

FUNDING OUR FUTURE

Thanks so much to the generous donors who support the research efforts in the Fisher Center. We are grateful. If you would like to make a donation, please give online at https://secure.jhu.edu/form/infdis.

WE THANK THE GENEROUS CONTRIBUTORS THAT HELP SUPPORT THE FISHER CENTER PROGRAM

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*IF YOU HAVE ANY QUESTIONS ABOUT GIVING, PLEASE CONTACT DONNA BOLIN AT **410-336-5761** OR BY EMAIL AT DBOLIN1@JHMI.EDU.*

+ RECENT PRESENTATIONS

Auwaerter, P. (December 7, 2020). Monoclonals for COVID-19 a 'Minor Contribution'. Medscape Infectious Diseases, Commentary [online video]. Medscape Infectious Diseases.

Auwaerter, P. (March 23, 2021). Highlights of 2020 IDSA/AAN/ACR Lyme disease Guidelines & 2020 IDSA Babesia Guidelines. Mid-Atlantic Tick Summit X, Maryland Department of Health, Center for Zoonotic and Vector-borne Diseases, held virtually online.

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Auwaerter, P. (June 14, 2021). A Quick Tour of the New Lyme Disease Guideline. Medscape Infectious Diseases, Commentary [online video]. Medscape Infectious Diseases.

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FisherFocus

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