COVID-19

Viral heart damage under scrutiny

Researchers are hunting for myocarditis in COVID-19 survivors

By **Jennifer Couzin-Frankel**

This fall, cardiologist Sam Mohiddin will embrace a new role—that of research subject. MRI scans of his heart at St. Bartholomew's Hospital in London, where he works, will help answer a pressing question: Do people who suffered a mild or moderate bout of COVID-19 months ago, as he did, need to worry about their heart health?

Fears that COVID-19 can cause the cardiac inflammation called myocarditis have grown, as doctors report seeing previously healthy people whose COVID-19 experience is trailed by myocarditis-induced heart failure. Mohiddin recently treated 42-year-old Abul Kashem, who had typical COVID-19 symptoms in April, including loss of smell and mild shortness of breath. A month later, he fell critically ill from severe myocarditis. "I'm just grateful to be alive," says Kashem, who spent more than 2 weeks in an intensive care unit. Why did this happen? he wonders.

How the virus might damage heart muscle is just one question researchers are now probing. Other studies are following people during and after acute illness to learn how common heart inflammation is after COVID-19, how long it lingers, and whether it responds to specific treatments. Researchers also want to know whether patients fare similarly to those with myocarditis from other causes, which can include chemotherapy and other viruses. In more than half of virus-induced cases, the inflammation resolves without incident.

But some cases lead to arrhythmia and impaired heart function, or, rarely, the need for a heart transplant. Because millions are now contracting the coronavirus, even a small proportion who suffer severe myocarditis would amount to a lot of people. "Are we going to have an increase of patients with heart failure secondary to this?" asks Peter Liu, a cardiologist and chief scientific officer of the University of Ottawa Heart Institute.

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> **Peter Liu**, University of Ottawa Heart Institute

Whether SARS-CoV-2, the virus that causes COVID-19, induces cardiac injury including myocarditis more often, or with greater severity, than other viruses is still unclear. Because SARS-CoV-2 can trigger an intense immune response throughout the body, survivors may be at heightened risk of cardiac inflammation. Another idea suggests COVID-19 patients might be prone to the condition because the virus enters cells by binding with the angiotensin-converting enzyme 2 (ACE2) receptor, which sits on heart muscle cells. But researchers caution against outrunning the data. "It's a good hypothesis, but it's not a tested one," says Leslie Cooper, a cardiologist at the Mayo Clinic in Jacksonville, Florida, about ACE2.

One reason it's hard to say whether COVID-19 poses a special risk of myocarditis is uncertainty about its prevalence after other infections. Echocardiogram studies after some influenza outbreaks suggest up to 10% of flu patients have transient heart abnormalities, Liu says. But such studies are scarce. "We don't scan patients after they had the flu," says Valentina Püntmann, a cardiologist at University Hospital Frankfurt.

Püntmann fueled concerns about myocarditis when she did just that with COVID-19 patients. Her team used MRI to scan the hearts of 100 COVID-19 patients an average of 71 days after they had tested positive. The scans showed cardiac abnormalities in 78 people, with 60 appearing to have active inflammation. Most also described lingering symptoms, such as fatigue and mild shortness of breath, leading Püntmann to wonder whether heart inflammation might be responsible.

Although the work by Püntmann and her colleagues, published in July in *JAMA Cardiology*, prompted alarming headlines, many researchers say it needs to be replicated. Cardiologists urge anyone with symptoms like shortness of breath or chest discomfort after COVID-19 to see a doctor, but they worry about a flood of healthy recovered people clamoring for heart assessments. "Here's the good news: We're going to find out" how likely cardiac injury is, says Matthew Martinez, director of sports cardiology at Morristown Medical Center.

Because of the physical demands of sports, team doctors need to be on guard for myocarditis. A paper in *JAMA Cardiology* last week reported a study of 26 athletes at Ohio State University after COVID-19; four had developed myocarditis. Professional sports leagues are also scanning the hearts of athletes who were infected with SARS-CoV-2. Those with myocarditis, re-

In Genoa, Italy, a recovered COVID-19 patient undergoes a test of heart function.

PHOTO: MARCO DI LAURO/STRINGER/GETTY IMAGES

gardless of whether they have symptoms, are benched, in part out of fear that myocarditis could lead to sudden death during intense activity. Martinez, who's helping coordinate the research for the National Basketball Association and Major League Soccer, predicts a flow of data on athletes over the coming months. "Those of us in this space are willing to ruin a Saturday or a Sunday to get this done."

He stresses, though, that even if researchers can clarify the average duration of myocarditis and its risks for a young athlete, those may be very different for a 50-year-old with obesity or high blood pressure, especially if they were sick enough with COVID-19 to be hospitalized. "In those individuals, I am going to be more cautious" and screen for heart injury, he says.

Others are pursuing clues to how COVID-19 can damage the heart, which might point to ways to head off the damage. "SARS-CoV-2 does challenge your immune system in unconventional ways," Liu says. Autopsies of heart tissue after COVID-19 have revealed inflammation in the heart's blood vessels instead of its muscle cells, the site of the inflammation caused by other infections. Another autopsy study found scattered death of heart cells, but the authors noted the mechanism of injury was unknown. "There's been a lot of discussion whether this is myocarditis" as typically defined, Liu says. Regardless, he and others hope for clinical trials to test whether preventive strategies, such as taking beta blocker drugs, might head off heart failure in someone flagged as high risk after COVID-19.

While Mohiddin volunteers for a study of survivors, he's also running one: a trial that aims to recruit 140 people while they are hospitalized with COVID-19 or soon after, 20 with severe myocarditis and the rest without. He and colleagues will look for abnormal T cell levels in the blood of people with myocarditis, which could help explain whether and how the immune system is causing cardiac injury. He is also exploring whether immune cell patterns in the blood presage myocarditis later.

Even if COVID-19 rarely causes serious myocarditis, one hypothesis is that mild cases could heighten the risk of heart disease years later. Scar tissue can form as myocarditis heals, and earlier work has shown residual cardiac inflammation portends worse heart health. As cardiologists, "We're in the business of identifying asymptomatic risk factors," such as hypertension, Mohiddin says. "It's not difficult to imagine that in the future, clinical practitioners will ask a new patient, 'Did you have COVID?'" ■

PHOTO: RON BROWN

Alan Minson says his Parkinson's symptoms improved after he started to use a "light helmet" in July 2019.

NEURODEGENERATIVE DISEASES

Trials begin for a new weapon against Parkinson's: light

Patients report benefits, but how near-infrared protects brain cells is unclear, and some scientists are skeptical

By **Gunjan Sinha**

Light therapy can help lift moods, heal wounds, and boost the immune system. Can it improve symptoms of Parkinson's disease, too? A first-of-its-kind trial scheduled to launch this fall in France aims to find out. In seven patients, a fiber optic cable implanted in their brain will deliver pulses of near-infrared (NIR) light directly to the substantia nigra, a region deep in the brain that degenerates in Parkinson's disease. The team, led by neurosurgeon Alim-Louis Benabid of the Clinatec Institute—a partnership between several government-funded research institutes and industry—hopes the light will protect cells there from dying.

The study is one of several set to explore how Parkinson's patients might benefit from light. "I am so excited," says neuropsychologist Dawn Bowers of the University of Florida College of Medicine, who is recruiting patients for a trial in which NIR will be beamed into the skull instead of delivered with an implant.

Small tests in people with Parkinson's and animal models of the disease have already suggested benefits, but some mainstream Parkinson's researchers are skeptical. No one has shown exactly how light might protect the key neurons—or why it should have any effect at all on cells buried deep in the brain that never see the light of day. Much or all of the encouraging hints seen so far in people may be the result of the placebo effect, skeptics say. Because there are no biomarkers that correlate well with changes in Parkinson's symptoms, "we are reliant on observing behavior," says neurobiologist David Sulzer of Columbia University Irving Medical Center, an editor of the journal *npj Parkinson's Disease*. "It's not easy to guard against placebo effects."

But proponents point to a Parkinson's therapy named deep brain stimulation (DBS), in which electricity of a specific frequency is applied to affected brain regions. Invented by Benabid more than 30 years ago, DBS has become a standard approach for treating tremors and other severe motor symptoms in Parkinson's patients even though its mode of action isn't entirely clear

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