From the Washington Post this week – An article on coronavirus autopsies.

When pathologist Amy Rapkiewicz began the grim process of opening up the coronavirus dead to learn how their bodies went awry, she found damage to the lungs, kidneys and liver consistent with what doctors had reported for months.

In dengue, a mosquito-borne tropical disease, she learned, the virus appeared to destroy these cells, which produce platelets, leading to uncontrolled bleeding. The novel coronavirus seemed to amplify their effect, causing dangerous clotting.

She was struck by the parallels: “Covid-19 and dengue sound really different, but the cells that are involved are similar.”

Autopsies have long been a source of breakthroughs in understanding new diseases, from HIV/AIDS and Ebola to Lassa fever — and the medical community is counting on them to do the same for covid-19, the disease caused by the coronavirus. With a vaccine probably many months away in even the most optimistic scenarios, autopsies are becoming a critical source of information for research into possible treatments.

When the pandemic hit the United States in late March, many hospital systems were too overwhelmed trying to save lives to spend too much time delving into the secrets of the dead. But by late May and June, the first large batch of reports — from patients who died at a half-dozen institutions — were published in quick succession. The investigations have confirmed some of our early hunches of the disease, refuted others — and opened up new mysteries about the pathogen that has killed more than 500,000 people worldwide.

Among the most important findings, consistent across several studies, is confirmation the virus appears to attack the lungs the most ferociously. They also found the pathogen in parts of the brain, kidneys, liver, gastrointestinal tract and spleen and in the endothelial cells that line blood vessels, as some had previously suspected. Researchers also found widespread clotting in many organs.

But the brain and heart yielded surprises.

“It’s about what we are not seeing,” said Mary Fowkes, an associate professor of pathology who is part of a team at Mount Sinai Health that has performed autopsies on 67 covid-19 patients.

Given widespread reports about neurological symptoms related to the coronavirus, Fowkes said, she expected to find virus or inflammation — or both — in the brain. But there was very little. When it comes to the heart, many physicians warned for months about a cardiac complication they suspected was myocarditis, an inflammation or hardening of the heart muscle walls — but autopsy investigators were stunned that they could find no evidence of the condition.

Another unexpected finding, pathologists said, is that oxygen deprivation of the brain and the formation of blood clots may start early in the disease process. That could have major implications for how people with covid-19 are treated at home, even if they never need to be hospitalized.

The early findings come as new U.S. infections have overtaken even the catastrophic days of April, amid what some critics say is a premature easing of social distancing restrictions in some states, mainly in the South and West. A new modeling study has estimated that about 22 percent of the population — or 1.7 billion

people worldwide, including 72 million in the United States — may be vulnerable to severe illness if infected with the virus. According to the analysis published this month in Lancet Global Health, about 4 percent of those people would require hospitalization — underscoring the stakes as autopsy investigators continue their hunt for clues.

At their best, autopsies can reconstruct the natural course of the disease, but the process for a new and highly infectious disease is tedious and requires meticulous work. To protect pathologists and avoid sending virus into the air, they must use special tools to harvest organs and then dunk them in a disinfecting solution for several weeks before they are studied. They must then section each organ and collect small bits of tissue for study under different types of microscopes.

One of the first American investigations to be made public, on April 10, was out of New Orleans. The patient was a 44-year-old man who had been treated at LSU Health. Richard Vander Heide remembers cutting the lung and discovering what was probably hundreds or thousands of microclots.

“I will never forget the day,” recalled Vander Heide, who has been performing autopsies since 1994. “I said to the resident, ‘This is very unusual.’ I had never seen something like this.”

But as he moved onto the next patient and the next, Vander Heide saw the same pattern. He was so alarmed, he said, that he shared the paper online before submitting it to a journal so the information could be used immediately by doctors. The findings caused a stir at many hospitals and influenced some doctors to start giving blood thinners to all covid-19 patients. It is now common practice. The final, peer-reviewed version involving 10 patients was subsequently published in the

Lancet in May.

Other lung autopsies — including those described in papers from Italy of 38 patients, a Mount Sinai Health study on 25 patients, a collaboration between Harvard Medical School and German researchers on seven and an NYU Langone Health study on seven — have reported similar findings of clotting.

Most recently, a study out this month in the Lancet's eClinicalMedicine, found abnormal clotting in the heart, kidney and liver, as well as the lungs of seven patients, leading the authors to suggest this may be a major cause of the multiple-organ failure in covid-19 patients.

The next organ studied up close was the heart. One of the most frightening early reports about the coronavirus from China was that a significant percentage of hospitalized patients — up to 20 to 30 percent — appeared to have a heart problem known as myocarditis that could lead to sudden death. It involves the thickening of the muscle of the heart so that it can no longer pump efficiently.

Classic myocarditis is typically easy to identify in autopsies, pathologists say. The condition occurs when the body perceives the tissue to be foreign and attacks it. In that situation, there would be large dead zones in the heart, and the muscle cells known as myocytes would be surrounded by infection-fighting cells known as lymphocytes. But in the autopsy samples taken so far, the dead myocytes were not surrounded by lymphocytes — leaving researchers scratching their heads.

Fowkes, from Mount Sinai, and her colleague, Clare Bryce, whose work on 25 hearts has been published online but not yet peer reviewed, said they saw some "very mild" inflammation of the surface of the heart but nothing that looked like myocarditis.

NYU Langone’s Rapkiewicz, who studied seven hearts, was struck by the abundance of a rare cell called megakaryocytes in the heart. Megakaryocytes, which produce platelets that control clotting, typically exist only in the bone marrow and lungs. When she went back to the lung samples from the coronavirus patients, she discovered those cells were too plentiful there, too.

“I could not remember a case before where we saw that,” she said. “It was remarkable they were in the heart.”

Vander Heide, from LSU, who reported preliminary findings on 10 patients in April and has a more in-depth paper with more case studies under review at a journal, explained that “when you look at a covid heart, you don’t see what you’d expect.”

He said a couple of patients he performed autopsies on had gone into cardiac arrest in the hospital, but when he examined them, the primary damage was in the lungs — not the heart.

Of all the coronavirus’s manifestations, its impact on the brain has been among the most vexing. Patients have reported a host of neurological impairments, including reduced ability to smell or taste, altered mental status, stroke, seizures — even delirium.

An early study from China, published in the BMJ, formerly the British Medical Journal, in March, found 22 percent of the 113 patients had experienced neurological issues ranging from excessive sleepiness to coma — conditions typically grouped together as disorders of consciousness. In June, researchers in France reported that 84 percent of patients in intensive care had neurological problems, and a third were confused or disoriented at discharge. Also this month, those in the United Kingdom found that 57 of 125 coronavirus patients with a new neurological or psychiatric diagnosis had had a stroke due to a blood

clot in the brain, and 39 had an altered mental state.

Based on such data and anecdotal reports, Isaac Solomon, a neuropathologist at Brigham and Women’s Hospital in Boston, set out to systematically investigate where the virus might be embedding itself in the brain. He conducted autopsies of 18 consecutive deaths, taking slices of key areas: the cerebral cortex (the gray matter responsible for information processing), thalamus (modulates sensory inputs), basal ganglia (responsible for motor control) and others. Each was divided into a three-dimensional grid. Ten sections were taken from each and studied.

He found snippets of virus in only some areas, and it was unclear whether they were dead remnants or active virus when the patient died. There were only small pockets of inflammation. But there were large swaths of damage due to oxygen deprivation. Whether the deceased were longtime intensive care patients or people who died suddenly, Solomon said, the pattern was eerily similar.

“We were very surprised,” he said.

When the brain does not get enough oxygen, individual neurons die, and that death is permanent. To a certain extent, people’s brains can compensate, but at some point, the damage is so extensive that different functions start to degrade.

On a practical level, Solomon said, if the virus is not getting into the brain in large amounts, that helps with drug development because treatment becomes trickier when it is pervasive, for instance, in some patients with West Nile or HIV. Another takeaway is that the findings underscore the importance of getting people on supplementary oxygen quickly to prevent irreversible damage.

Solomon, whose work was published as a June 12 letter in the New England Journal of Medicine, said the findings suggest the damage had been happening over a longer period of time, which makes him wonder about the virus's effect on people who are less ill. "The big lingering question is what happens to people who survive covid," he said. "Is there a lingering effect on the brain?"

The team from Mount Sinai Health, which took tissue findings from 20 brains, was also perplexed not to find a lot of virus or inflammation. However, the group noted in a paper that the widespread presence of tiny clots was "striking."

"If you have one blood clot in the brain, we see that all the time. But what we're seeing is, some patients are having multiple strokes in blood vessels that are in two or even three different territories," Fowkes said.

Rapkiewicz said it is too early to know whether the newest batch of autopsy findings can be translated into treatment changes, but the information has opened new avenues to explore. One of her first calls after noticing the unusual platelet-producing cells was to Jeffrey Berger, a cardiac specialist at NYU who runs a National Institutes of Health-funded lab that focuses on platelets.

Berger said the autopsies suggest anti-platelet medications, in addition to blood thinners, may be helpful to stem the effects of covid-19. He has piloted a major clinical trial looking at optimal doses of blood thinners to examine that question as well.

"It's only one piece of a very big puzzle, and we have a lot more to learn," he said. "But if we can prevent significant complications and if more patients can survive the infection, that changes everything."