The coronavirus pandemic has affected everyone, but now some are worried that children with a rare disease could be at increased risk from COVID-19.

As infections rose in the United Kingdom and Italy, doctors there began to notice children coming in with symptoms similar to Kawasaki disease, a rare inflammatory syndrome. Now there are almost a hundred cases in New York and at least three deaths, and geneticists are teaming up with the state’s health department to try and get to the bottom of it. So what is Kawasaki disease? Why are doctors looking at a possible link between it and COVID-19? And what are scientists doing to get answers?

Dr. Jane Burns is the director of the Kawasaki Disease Research Center at UC San Diego and an expert who researched a treatment for Kawasaki disease now used around the world. When children in New York, the U.K., and Italy started coming into hospitals with symptoms similar to the inflammatory disease, she found the numbers highly unusual.

“I talked to one of our collaborators in Queens who at one point over the weekend had 12 regular Kawasaki disease patients in her hospital on the ward at the same time. I’ve been studying this disease for 40 years and I have never seen that many. My world record was five,” she said. “That’s clearly extraordinary. So something’s going on and the hypothesis that we are collaborating with many other groups across the country and across the world to try to test is: Is the SARS-CoV-2 virus one of many triggers for Kawasaki disease?”

Kawasaki disease is a pediatric inflammatory syndrome that presents with a number of symptoms. Children with the disease often come into the doctor’s office with fevers, rashes, swollen lymph glands, red eyes, dry, cracked lips, and a swollen, bumpy tongue. But what makes the disease so worrying is that it causes inflammation that can lead to vascular damage. The disease causes an overreaction of the immune system to attack the lining of the blood vessels, causing them to dilate and become inflamed. In severe cases, some children can develop potentially lethal coronary aneurysms.

From a handful to dozens: Reports of a possible link between COVID-19 and Kawasaki disease in children first emerged in Europe in late April, when physicians began noticing two things happening in areas like northern Italy and London, which have been hit especially hard in the coronavirus pandemic.

First, doctors began noticing a greater number of cases of children showing up for treatment with classic signs of Kawasaki disease. Separately, health officials in the U.K. began to notice a group of more severely ill kids with an “apparently new condition” that officials called Pediatric Inflammatory Multisystem Syndrome, or PIMS. Guidance put out by the Royal College of Pediatrics and Child Health describes PIMS as a collection of symptoms including persistent fever, inflammation, multi-organ dysfunctions, or symptoms that are similar to Kawasaki disease or toxic shock syndrome.

A positive diagnosis for COVID-19 isn’t necessary to qualify as a potential PIMS case and guidance from the U.K.’s National Health Service indicated that “Despite the current COVID19 pandemic, most patients are testing negative for the SARS-CoV-2 virus” when given molecular tests, which check for current infection.

In May, New York Gov. Andrew Cuomo announced that health officials in the state were investigating 85 cases of children afflicted with PIMS-like symptoms similar to Kawasaki disease.

Guidance from the New York state health department suggested a closer correlation between PIMS and COVID-19 because “the majority of patients who have presented with this syndrome” tested positive for COVID-19 antibodies, which, unlike molecular tests, can detect infection even after the virus has left the body. (A smaller number of patients tested positive for current infection, according to the guidance.)
The greatest fear: Before the pandemic, Kawasaki disease was known as a somewhat rare and frightening occurrence in children, but one with a relatively low instance of death—about 1 percent of acute cases in the U.S.

The number of deaths associated with suspected PIMS cases is also small but still worrying. A study of the first eight patients who presented in the U.K.—an “unprecedented” number in such a short time for a rare disease—prompted the country’s alert to hospitals and doctors. The study, published in *The Lancet*, noted that one of the children experienced a coronary aneurysm and another died. In New York, state officials have linked three deaths to PIMS and say they’re investigating another two.

Mystery on top of mystery: “Prior to this, we would have said the only thing on planet earth that gives you coronary artery aneurysms in an otherwise previously healthy child who goes back to being healthy is Kawasaki disease,” said Dr. Burns, the Kawasaki Disease Research Center director. But Burns, who first researched the intravenous antibody treatment for Kawasaki disease now used around the world, insists that she deals in facts, not opinions, and so far there aren’t enough to draw any hard conclusions about causes or linkages.

But there are a number of strange occurrences, both among recent suspected PIMS patients and normal Kawasaki disease cases.

One of the biggest challenges in finding out whether there’s any connection between Kawasaki disease and COVID-19 is the important gaps in our understanding of the disease and what causes it.

Right now, scientists think that there’s a genetic component to the disease. While genetics may predispose children toward the disease, researchers think that some other still-unknown factors might trigger its onset.

“We have this condition called Kawasaki disease that is new after World War II in Asia and was extremely rare in the Western world before World War II,” explained Burns. “Kawasaki disease was something new. That means it has to be created in genetically susceptible children by something new in the environment.”

For a while, some theorized that a chemical in carpet cleaner could be a trigger for the disease, but studies have found no connection between children with Kawasaki and the chemical.

Both COVID-19 and Kawasaki disease involve overactive immune responses that can cause damage to vital organs, but despite the similarity in symptoms, researchers caution that it’s too early to say whether they’re linked.

“From the descriptions of what I’ve read about the SARS-CoV-2 reports, they sound worse than Kawasaki,” said Dr. Mark Hicar, an expert on pediatric infectious diseases at the University of Buffalo who’s studied Kawasaki disease. “I’m more concerned about those inflammatory conditions.”

Answers in the genes? To help get to the bottom of the mysterious pattern of children with inflammatory syndromes, researchers at the New York Genome Center and Rockefeller University have partnered with New York state’s health department to launch a study of children with Kawasaki-like illnesses in the state.

“The genome center has offered to sequence the patients that have this. We offer a whole genome sequencing clinical tests for genetic diseases,” said Michael Zody, a computational biologist at the Genome Center.

“The idea is to offer that to these patients and their families to try to see if we can identify whether there is a recurrent genetic cause that can be linked to these cases,” he said. “The hope would be that we would actually be able to identify one or more underlying genetic causes that would then be able to help us test for people who might be susceptible to this, but also that understanding the genetic cause might point to what’s going wrong in people when they have this reaction to the infection.”

Those answers, geneticists hope, might be able to provide researchers with the data they need to help develop new treatments so that kids can be the one group the world can protect from the global pandemic.