A poliolike illness is on the rise again. But why?

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At first, it seemed like just a bad cold, with a fever that came and went.

Then one day, when Scarlett Camburn woke from her nap, the Havertown, Pa., toddler was unable to move her right arm.

Panicked, parents Andrea and Chris Camburn rushed the little girl to an urgent care center in King of Prussia operated by Children's Hospital of Philadelphia, and from there to the hospital's emergency room in West Philadelphia. X-rays showed that Scarlett, a few days shy of her second birthday in August 2016, had no broken bones. But an MRI on a future visit revealed an alarming sign: damage to her spinal cord.

The Camburns would soon learn that Scarlett was among dozens of children around the country that year whose arms or legs suddenly went limp—evoking memories of polio, a scourge eliminated in the United States decades ago.

One of those children was Chase Kulakowski, of Dyer, Ind., age 15 months. Same pattern: had a cold, woke up from a nap, couldn't use his right arm.

"His arm was totally limp," said his mother, Jessica.

The inflammation in Scarlett's spinal cord eventually was attributed to a virus, called enterovirus D68, that had infected many of the other children. But for some patients, including Chase, no virus—or other

cause—was found.

This fall, it's happening again. Last week, the U.S. Centers for Disease Control and Prevention said it had confirmed 72 cases of sudden muscle weakness or paralysis so far in 2018, including six in Pennsylvania and three in New Jersey.

The disease is often referred to as mysterious, given that some victims are found to be infected with D68 while others are not, and officially, the CDC says the cause for most cases remains unknown. But a core group of academic researchers tracking the disease is fairly certain that the virus, which can be hard to detect, is the primary culprit.

They're just not sure what to do about it.

And they are worried it could get worse.

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The first warning signs came in 2012, when the California Department of Public Health learned that a handful of children in the state were suffering from sudden, unexplained weakness in the arms or legs. The agency launched a statewide surveillance program, and by year's end found that among 10 patients, two had been infected with enterovirus D68.

First identified in 1962, D68 was known only to cause respiratory symptoms. But the two cases of muscle weakness were cause for concern. Those symptoms were similar to what happens with polio, which also is caused by an enterovirus. Was D68 able to cause similar harm?

Two years later, things went national. By the end of 2014, 120 people in

34 states were confirmed to have the condition, called acute flaccid myelitis. Again, almost all were children. Again, some were found to be infected with D68. Many were not, yet by the end of the year, an informal working group of prominent physicians was confident the virus played a key role. Symptoms ranged from moderate weakness to complete paralysis of the affected limbs, more often in the arms than legs.

In Dallas, researchers at UT Southwestern Medical Center had recently been awarded a federal grant to study a broader category of pediatric paralysis, so they were "up and running" to track the unusual new cases, neurologist Benjamin M. Greenberg said. Among the questions: How much did children recover the use of their limbs? Which treatments seemed most effective? What type of spinal-cord damage was seen on their MRI scans?

The condition remained rare, but the words "polio-like" in media headlines stoked public fears, bringing to mind a dreaded disease that was far worse in scope. Polio, eliminated in the United States through widespread vaccination, paralyzed thousands of people each year in the early 1950s.

Keen to make sure polio had not returned, the CDC began testing patients' fecal samples for the virus that causes the real thing. After all, polio still emerges periodically in a handful of other countries, said Sarah Hopkins, a neurologist at Children's Hospital of Philadelphia.

"With some people opting not to vaccinate their children and international travel, there always is that worry," Hopkins said. "It's important for us to rule it out."

None of the new cases tested positive for polio. But while some patients were found to be infected with D68, some of the children did not test

positive for anything. What was causing their paralysis?

Two years later, in 2016, the number of patients with muscle weakness spiked again.

Physicians tracking the illnesses suspected that the enterovirus was to blame even in patients where it was not found. That's because the genetic information in an enterovirus is stored as RNA, not DNA, which makes it harder to isolate from a patient. And by the time muscle symptoms appear, the patient's body may have cleared itself of the virus.

"The fact that kids are testing negative on a regular basis should not surprise anybody," said Greenberg, of UT Southwestern's O'Donnell Brain Institute.

So CHOP and some other hospitals set up protocols to obtain and test nasal swabs as soon as possible in patients with sudden muscle weakness or paralysis—maximizing their chances of finding the virus if it was there. Sure enough, most patients at CHOP that year had D68 in their respiratory secretions, Hopkins said. And the virus popped up repeatedly elsewhere in the country, though in a handful of cases, patients were found to be infected with a different enterovirus, dubbed A71.

At the end of 2016, the CDC had confirmed 149 cases of patients with sudden muscle weakness or paralysis in 38 states and Washington, D.C. By definition, those included in the total had experienced a sudden onset of symptoms and had suffered damage to the internal gray matter of the spinal cord—interrupting the nerve signals needed to activate an arm or leg.

The cases tended to emerge in geographic clusters, supporting the theory that the symptoms were caused by an infectious agent—a virus. And, like illnesses caused by some other viruses, the cases of muscle weakness

spiked in the fall—consistent with an infectious agent that thrives in cooler temperatures. Even the two-year pattern made sense. It is common for viruses to ebb and flow on a multi-year cycle as they travel through a population.

Yet another layer of evidence for a viral cause came from the University of Colorado, where researchers injected mice with strains of D68. Just as in human patients, the animals' limbs became paralyzed.

To Greenberg, that represented a convincing, three-pronged case that the enterovirus was to blame for the biennial spikes in acute flaccid myelitis.

"We know the virus can do it" in mice, he said. "We know it's present in humans. And we know the epidemiological pattern fits that of an infection."

But two mysteries remained.

When Chase Kulakowski got his cold in October 2016, his stepsister had the same symptoms: a runny nose and a cough. By all appearances, they were infected with the same virus.

Yet her arms and legs were fine, whereas Chase could not move his right shoulder and arm.

"What makes him different?" his mom asked.

Likewise at Scarlett Camburn's preschool, there were the usual runny noses, but nobody else had her muscle symptoms. Why?

Those are good questions, scientists say.

At the Johns Hopkins Bloomberg School of Public Health, researchers

are exploring whether some genetic quirk might make certain infected people more likely to develop acute flaccid myelitis.

The team has gathered DNA samples from more than 60 willing families—including patients, siblings, and parents, said Priya Duggal, director of the school's genetic epidemiology program. Any two non-identical siblings share 50 percent of their DNA, on average, so one child might inherit some mutation that raises the risk of virally induced paralysis while a sibling does not, she said. Or such a mutation could have occurred in a child sporadically—popping up for the first time in that generation.

To date, Duggal said, there have been no reports of two children in the same household developing acute flaccid myelitis.

"It can't just be the virus," Duggal said. "Otherwise, we'd have schools filled with children that were all paralyzed."

If the virus is causing the paralysis, it makes sense that the symptoms would occur primarily in children, physicians say. Most people become infected with a variety of enteroviruses during childhood without symptoms and are therefore immune to them as adults.

A similar lack of symptoms was seen in most people infected with polio. One in four people infected with polio experienced flu-like symptoms that went away on their own, and fewer than 1 percent of infections led to irreversible paralysis. But when they did, the consequences could be deadly, as the disease can affect muscles involved in breathing.

Then there's the mystery of the virus itself.

In addition to injecting mice with D68 strains that were isolated from the 2014 outbreak, the Colorado researchers injected animals with strains of

the virus that had infected humans in 1962.

Just like the humans infected in 1962, mice in the latter group did not become paralyzed. The strains of virus from the two eras, five decades apart, look very similar but apparently evolved in some consequential way, acquiring the ability to harm the spinal cord, Greenberg said. And as with any virus, it will evolve again.

"Something changed," he said. "This is a very rare event, and I acknowledge it's a rare event, but I am also asking the scientific and public-health community to recognize that doesn't mean it's going to be a rare event forever."

As the detective work continues, physicians have developed effective treatments for patients. At CHOP, Scarlett was given intravenous immunoglobulin—a substance that can help reduce swelling in the spinal cord. Elsewhere, physicians have opted to administer steroids, though there is disagreement as to when that is appropriate.

After months of therapy, Scarlett also underwent surgery at CHOP called a nerve transfer. Chase did the same at Shriners Hospital for Children in Philadelphia, traveling there from Indiana.

The procedure allows physicians to reactivate a paralyzed limb by connecting it to healthy nerves that have been rerouted from elsewhere in the body, said Dan Zlotolow, who performs the surgeries at Shriners.

Patients must then adapt to the rewiring—learning how nerve signals that once controlled, say, a rib muscle will now operate the elbow. Early on, a patient may find that during a sneeze or a deep breath, the elbow will bend, the surgeon said.

"Over time, your brain will figure out that is not what should happen,"

Zlotolow said.

Now 4 years old, Scarlett has regained the use of her right arm but still has trouble making a fist, as her hand muscles deteriorated during the months of receiving no nerve signals. Next year, she will have another operation, in which surgeons will transfer a tendon to her hand from elsewhere in the body.

Her family has nicknamed her right arm "Lucky—in the Disney movie "Finding Nemo," the title character's lucky right fin is small and weak. Scarlett's parents both got matching tattoos of the orange fish on their right arms. They seek solace from an active support group on Facebook, which includes parents of many of the nearly 400 children recovering from acute flaccid myelitis.

"We felt so isolated, and now to realize there's a whole community of us," Andrea Camburn said.

She, Jessica Kulakowski and other parents in the support group worry that the federal government is not doing enough to address the disease.

Greenberg, the UT Southwestern neurologist, describes the experience for families as "a horrific nightmare," and agrees that the medical community should do more. Better tests for diagnosis are needed, he said. More should be invested in researching the best treatments, especially if the virus becomes more widespread.

"I get asked the question all the time: Should parents be worried?" he said. "In 2018, no, your kids are going to get a cold, and they're going to be fine" in the overwhelming majority of cases. "As a society, we should ask, 'Should we be worried about 2028 or 2038?'"

Duggal, the Johns Hopkins epidemiologist, agrees. Given that

enterovirus D68 is the likely culprit, she said society should consider investing in the same weapon that stopped polio: a vaccine.

"We've been here for four years looking at these patients, watching the devastation," Duggal said. "This is the third round of it. We don't want to be looking at it in 2020, saying, 'There's a mystery illness.' We want to be looking at it in 2020 saying, 'We're making headway.'"