Why the mystery hepatitis in children may have been here all along

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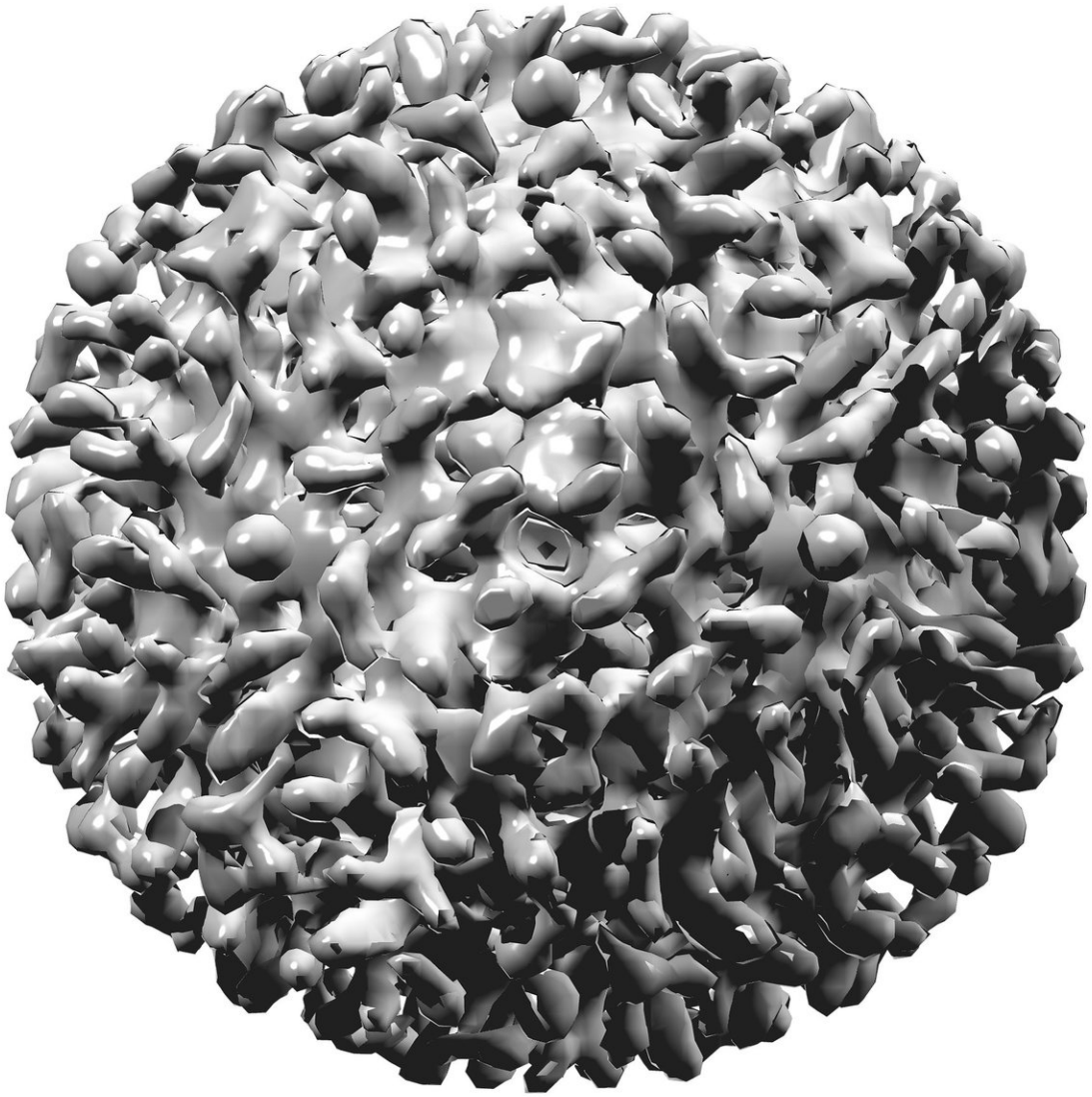

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The children typically show up at hospitals scattered across the country, one or two at a time, with symptoms like unexplained vomiting, diarrhea and jaundice. These are the classic signs of hepatitis—inflammation of the liver—yet in many cases, no cause is ever identified.

That's why the nation's disease detectives are so intrigued by the evidence emerging from more than 200 pediatric hepatitis cases dating back to October, including a handful from Pennsylvania, New Jersey, and Delaware.

Close to half of the children, including an initial nine identified in Alabama, tested positive for an adenovirus—a type of virus not normally associated with hepatitis.

It's possible that the virus has been responsible all along for many of the cases for which no cause is ever identified, CDC officials said at a briefing. An investigation remains underway, in cooperation with officials in 32 other countries where cases have been reported. As of Friday, 650 cases are under investigation worldwide, the World Health Organization said.

The CDC also is investigating whether some sort of "co-factor" is involved, causing the children to become sicker from the adenovirus than would otherwise be the case. Among the early possibilities considered: the virus that causes COVID-19.

And investigators are looking for other possible causes of the hepatitis, such exposure to drugs, toxins, or food, but so far an adenovirus infection remains a leading theory, said Jay Butler, the CDC's deputy

director for infectious diseases. The unusual cluster last fall in Alabama was the first clue.

"This is the type of shoe-leather epidemiology that our disease detectives are trained to do," he said.

Six of the U.S. children died, and 15 have needed liver transplants, whereas symptoms were moderate or mild in the rest. The CDC did not specify where the six deaths occurred in order to protect patient privacy, agency officials said.

St. Christopher's Hospital for Children has reported two cases to the Philadelphia Department of Public Health, said Janet Chen, section chief of infectious diseases at the North Philadelphia hospital. She noted that the likelihood that COVID plays a role in the unknown hepatitis seems to be weakening. But it's too soon to rule it out entirely.

"If the last two years have taught us anything, COVID is involved in a lot of things," she said.

The liver is a complex organ, ridding the body of toxins while making other substances that are essential for survival, among them proteins used in clotting blood. The organ also is involved in producing cholesterol, and it stores energy in the form of glucose.

Hepatitis is a catchall term for inflammation in the organ. And while other viruses are known to cause it (the hepatitis viruses A, B, and C are the most common), adenoviruses have been implicated only in cases where the child's immune system is compromised.

The unusual cluster last fall in Alabama pointed epidemiologists in the direction of the adenovirus.

In cases where the virus could be subjected to genetic testing, labs have identified a specific type called adenovirus 41.

For children whose samples are no longer available for viral testing, the other case details are still valuable in establishing the scope of disease, said Jim Squires, an associate professor of pediatrics in the division of gastroenterology and hepatology at UPMC Children's Hospital of Pittsburgh.

That hospital has identified several such cases that meet the CDC's broad definition for inclusion: children in whom a type of liver enzyme was elevated, he said.

"It's getting a denominator of how many cases are out there," said.

Still, Squires agreed with CDC officials that the adenovirus was a possible culprit in the recent cases.

Yet uncertainty remains. Generally, the adenovirus was not found in the children's livers, but in their blood.

As more and more hepatitis cases have been identified, COVID is looking less likely as a contributing factor. The percentage of cases in children who turned out to have a recent or current infection with the coronavirus has dipped below 20%, the CDC's Butler said.

If the adenovirus turns out to be the prime culprit, it could, in theory, be prevented with the same tool we've used against COVID: a vaccine.

A vaccine that protects against two other types of adenoviruses is recommended for members of the U.S. military, though no adenovirus vaccine is on the recommended schedule for children.

"I think everything's on the table," said Chen, of St. Christopher's Hospital for Children. "We have to kind of wait and see how this plays out."