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## Mysterious hepatitis outbreak sickens young children in Europe as CDC probes cases in Alabama

Researchers suspect an adenovirus may be involved, but are still searching for the cause of illness

15 APR 2022 | 10:45 AM | BY MEREDITH WADMAN



La Paz University Hospital in Madrid admitted a 22-month-old with acute hepatitis, *El País* newspaper reported this week. The child is one of dozens of European and U.S. children with serious hepatitis of unknown cause. [BESTRAVELVED/ALAMY STOCK PHOTO](#)

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Puzzled scientists are searching for the cause of a strange and alarming outbreak of severe hepatitis in young children, with 74 cases documented in the United Kingdom and three in Spain. Clinicians in Denmark and the Netherlands are also reporting similar cases. And in the United States, the Centers for Disease Control and Prevention (CDC) said late yesterday it is investigating nine cases in Alabama.

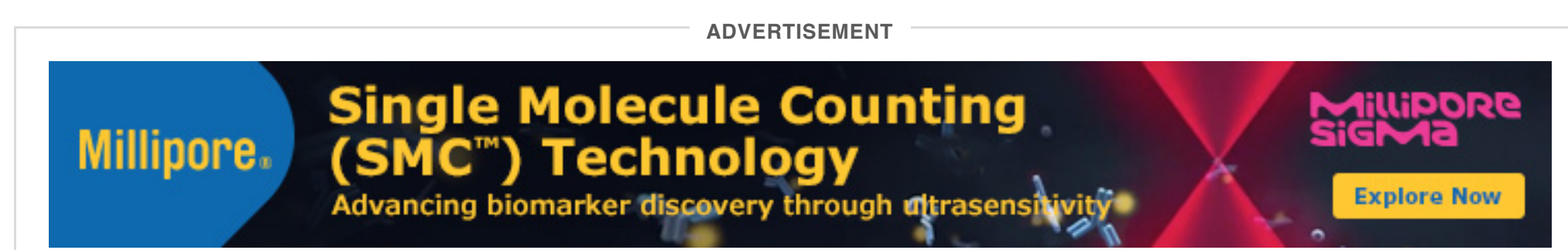
Viruses can cause hepatitis, an inflammation of the liver, but otherwise-healthy children rarely become seriously ill. As of 12 April, none of the U.K. or Spanish children have died, but some are very sick: All have been admitted to hospitals and seven required liver transplants, **six of them in the United Kingdom**, according to a World Health Organization (WHO) statement issued today. Two of the nine affected children in Alabama have required liver transplants, the state's Department of Public Health **announced** this afternoon.

The leading theory is that an adenovirus, a family of viruses that more typically cause colds, is the culprit—up to half of the sickened children in the United Kingdom tested positive for such a virus, as did all the children in Alabama. But so far, the evidence is too thin to resolve the mystery, researchers and physicians say.

"This is a severe phenomenon," says Deirdre Kelly, a pediatric hepatologist at Birmingham Children's Hospital in the United Kingdom. "These [were] perfectly healthy children ... up to a week ago." Not all the news is bad, however. "Most of [the children] recover on their own," Kelly notes.

"This should be taken seriously," WHO's Regional Office for Europe wrote in an emailed statement. "The increase is unexpected and the usual causes have been excluded."

Scottish investigators first identified the outbreak on 31 March, when they alerted Public Health Scotland to a cluster of 3- to 5-year-olds admitted to the Royal Hospital for Children in Glasgow in the first 3 weeks of March. Each was diagnosed with severe hepatitis of unknown cause. Typically, Scotland sees fewer than four such cases annually, the investigators wrote in a **paper published yesterday**. But there have been 13 cases in Scottish children as of 12 April, all but one in March and April.



Kelly, who works at one of England's three centers for pediatric liver disease and transplantation, says that since the start of this year, her unit has seen 40 cases of childhood hepatitis of uncertain cause. Over the same January to April period in 2018, her unit saw only seven such children.

Most of the U.K. children are 2 to 5 years old, according to a **statement** issued on 8 April by the UK Health Security Agency. The European Centre for Disease Prevention and Control **issued a public alert** on 12 April about the U.K. outbreak, noting that vomiting and jaundice—yellowing of the skin and the whites of the eyes—are common symptoms.

Early hypotheses about what might be making the children sick included a toxic exposure from food, drinks, or toys, but suspicion now centers on a virus. None of the U.K. or Spanish kids had the hepatitis A, B, C, or E viruses, typical infectious causes of the disease. But a handful of children tested positive for SARS-CoV-2 infection shortly before or upon hospital admission; none had received a COVID-19 vaccine. In addition, as many as half had adenovirus, a common virus passed by respiratory droplets and from touching infected people or virus on surfaces. It can cause vomiting, diarrhea, conjunctivitis, and cold symptoms but rarely causes hepatitis.

"The leading hypotheses center around adenovirus—either a new variant with a distinct clinical syndrome or a routinely circulating variant that is more severely impacting younger children who are immunologically naïve," the Scottish investigators wrote.

Isolation of the youngest children during the pandemic lockdown may have left them immunologically vulnerable because they haven't been exposed to the multiplicity of viruses, including adenoviruses, that typically attend toddlerhood. "We are seeing a surge in typical childhood viral infections as children come out of lockdown, [as well as] a surge in adenovirus infections"—but can't be sure that one is causing the other, says Will Irving, a clinical virologist at the University of Nottingham.

Researchers continue to study other possibilities. For example, the immunological effects of a prior episode of COVID-19 might have left children more vulnerable to infection or the illness could be a long-term complication of COVID-19 itself. An unidentified toxin has also not been ruled out.

All the cases might not have a single cause, cautions Jim McMenamin, an epidemiologist who heads the infection service of Public Health Scotland. "It's awfully important that we ensure we are looking for everything, that we are not confining ourselves to saying this is simply one viral cause."

In the United States, CDC is helping the Alabama Department of Public Health investigate nine cases of hepatitis in children ranging in age from 1 to 6 years old and who also tested positive for adenovirus. The cases have occurred since October 2021, Kristen Nordlund, a CDC spokesperson, wrote in the statement emailed to *ScienceInsider* last night.

"CDC is working with state health departments to see if there are additional U.S. cases, and what may be causing these cases," she wrote. "Adenovirus may be the cause for these, but investigators are still learning more—including ruling out the more common causes of hepatitis."

Wes Stubblefield, a district medical officer with the Alabama Department of Public Health, said in an interview today that the most recent case in Alabama occurred in February, and that five of the nine children tested positive for adenovirus-41, a strain that commonly causes gastroenteritis.

Meanwhile, in Spain, the government of the Madrid region announced on 13 April that three regions—Madrid, Aragón, and Castilla-La Mancha—had each reported a case of severe hepatitis of unknown origin in young children. One child has received a liver transplant.

Physicians at major pediatric liver centers in the Netherlands and Denmark told *ScienceInsider* yesterday they are seeing similar trends. "There are children that are very sick and have been referred for transplantation," says Ruben de Kleine, a pediatric liver transplant surgeon at University Medical Center Groningen. "We have assessed a similar number of kids for transplantation within the first 4 months of 2022 [to what we] normally do in a whole year."

At Copenhagen University Hospital, too, "we have more cases with [acute liver failure] than we normally have," says pediatric hepatologist Marianne Hørbj Jørgensen. No children there have needed transplants.

Hørbj Jørgensen and de Kleine both stress that parents should not panic. To date, clinicians have identified small numbers of cases in their countries where, combined, more than 230,000 infants are born each year.

**Update, 15 April, 3 p.m.:** This story has been updated to include more details about the Alabama cases.

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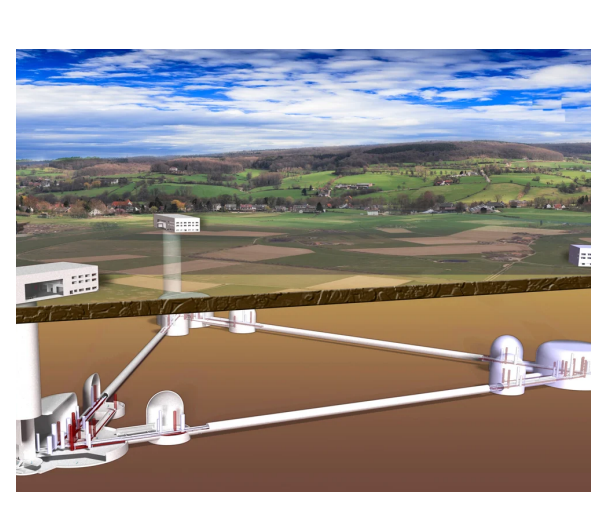


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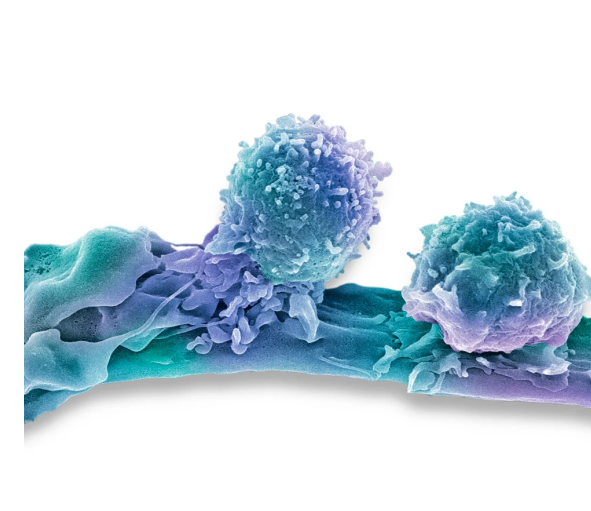
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