Still Few Answers as Kids Hepatitis Outbreak Spreads

Nearly 200 cases of pediatric hepatitis have now been reported in more than a dozen countries and several states.

May 1, 2022 By Liz Highleyman

Researchers and health officials are racing to determine the cause of an unexplained outbreak of pediatric hepatitis as more cases are reported around the world every day. Unfortunately, the mysterious cluster of cases is also spawning an outbreak of misinformation.

“People are speculating till they’re blue in the face, but all we have is a heap of correlations and no certain cause,” Isaac Bogoch, MD, of the University of Toronto, told the Financial Times.

As Hep previously reported, a cluster of pediatric hepatitis cases was first detected two weeks ago in the United Kingdom. At that time, 60 cases in England and 13 cases in Scotland were under investigation, mostly among children ages 2 to 5. Soon thereafter, nine cases were reported in Alabama, dating back to last fall.

Once health officials knew what to look for, more reports began flooding in. The unexplained illness has now been found in more than a dozen countries, including Canada, Israel, Japan, Singapore and several European nations. Nearly 200 kids have been affected, ranging from 1 month to 16 years old, though most are preschool age. At least 17 children required liver transplants and at least one has died, according to a World Health Organization bulletin that is now a week out of date. Although it’s being called an “outbreak,” many of these cases are not new but rather are being identified retrospectively.

CDC nationwide health alert: A cluster of children identified w/ #hepatitis and #adenovirus infection. Physicians should be alert for symptoms & report any suspected hepatitis cases of unknown origin to their

local and state health departments.

https://t.co/vzi2xjmKRh

— CDC (@CDCgov) April 21, 2022

In the United States, the Centers for Disease Control and Prevention (CDC) issued a nationwide health alert on April 21, asking physicians to be on the lookout for possible cases. So far, more than two dozen cases have been reported in states including Alabama, California, Delaware, Illinois, New York, North Carolina and Wisconsin.

What's Causing the Outbreak?
Hepatitis simply means inflammation of the liver, and it can have many causes. Viral hepatitis (including hepatitis A, hepatitis B and hepatitis C) is most familiar. The condition can also be caused by fatty liver disease, heavy alcohol use, toxins, autoimmunity and certain inherited conditions.

Signs and symptoms of hepatitis—regardless of cause—include elevated liver enzymes, jaundice (yellowing of the skin and eyes), dark-colored urine and pale-colored stools. It can also produce less specific symptoms, such as fatigue, fever, loss of appetite, abdominal pain, nausea and vomiting.

While the cause of the pediatric hepatitis outbreak remains unknown, multiple suspects are under investigation. Press reports and social media discussions have posited that it may be a COVID-19 complication or a result of COVID lockdowns, but neither has been confirmed by available evidence.

Several leading hypotheses were described during an emergency session at the recent European Society of Clinical Microbiology and Infectious Diseases conference in Lisbon and laid out in a briefing document from the U.K. Health Security Agency.

There are so many uncertainties. Working hypotheses include:

-adenovirus coinfection w/ other infections

-factors increasing susceptibility & severity of adenovirus infection

-toxin, drug or environmental factors

There is still more work to be done #ECCMID2022

pic.twitter.com/byDbWYZNIk

— Muge Cevik (@mugecevik) April 25, 2022

First, some causes can be ruled out:

- The affected children tested negative for well-known hepatitis viruses (A, B, C, D and E).
- Few, if any, of the affected children received COVID-19 vaccines because kids this age are not yet eligible in most countries.
- Most of the children are over age 2, meaning their mothers generally would not have been pregnant or breastfeeding during the COVID pandemic.
- The adenoviruses used as vectors in some COVID vaccines (adenovirus type 26 in the J&J vaccine, types 26 and 5 in the Russian Sputnik vaccine and a chimpanzee adenovirus in the AstraZeneca-Oxford vaccine) are inactivated so they won't cause disease.
- So far, no shared exposures to potential toxins, contaminated food, drugs or other environmental factors have been identified.

The leading suspect is adenovirus type 41, according to a majority of health experts investigating the outbreak. More than 50 types of adenovirus can cause infection in humans. Though these viruses are best known for causing the common cold, this particular type is associated with gastrointestinal illness.

A majority of the affected children had detectable adenovirus in their blood, and type 41 was most common among those with available molecular sequencing results. However, in the Alabama cases, adenovirus was not found in liver biopsy samples.

Adenoviruses are widespread, and infection is common in children and adults. This raises the question of why they have not previously been linked to liver disease outbreaks. There have been prior reports of adenoviruses causing hepatitis, especially in immunocompromised people, but this appears to be rare.

It's possible that a new or previously unrecognized adenovirus strain could be the culprit, or an

adenovirus could be interacting with another pathogen to cause more severe illness.

Some experts, including the authors of a Eurosurveillance report about the cases in Scotland, have suggested that reduced exposure to germs due to “restricted social mixing” during the COVID-19 pandemic may have left children with inadequate immunity. But this raises the question of why cases are cropping up in areas with and without lockdowns, and at varying intervals after COVID restrictions ended.

What About COVID?

The emergence of an unexplained pediatric hepatitis outbreak during a global pandemic has led many to wonder whether SARS-CoV-2, the coronavirus that causes COVID-19, is to blame.

SARS-COV-2 has been detected in only a minority of children involved in the outbreak. But the virus usually clears after several weeks, and the absence of viral material at present does not mean a child did not have COVID in the past. Indeed, the rising prevalence of COVID—a recent CDC study found 75% of children in the U.S. have SARS-CoV-2 antibodies—suggests that many of these kids likely were infected.

SARS-CoV-2 is not just a respiratory virus, and it has become increasingly clear that it can damage organs throughout the body. Over the course of the pandemic, there have been reports of potentially COVID-related liver disease in adults and children.

In August 2020, for example, researchers in New York City reported that 19 out of 44 pediatric patients with COVID-related multisystem inflammatory syndrome in children (MIS-C) had liver inflammation. Another U.S. team recently reported on four previously healthy children who presented with severe hepatitis as the primary manifestation of COVID-19. And in India, researchers reported 37 cases of what they called “COVID-19 associated hepatitis in children” during the second wave in that country, 10 of which were severe.

This raises even more questions. Given that the pandemic is in its third year, why would an outbreak of hepatitis in kids only be showing up now? In part, this may be because clinicians and health officials are now looking for it, and sporadic cases seen over the past two years may in fact be the same condition.

Perhaps SARS-CoV-2 is interacting with an adenovirus (several affected children tested positive for both the coronavirus and adenovirus type 41). Maybe there’s something unique about the omicron variant that makes it more likely to cause liver disease in kids—or perhaps the culprit is a new, unrecognized SARS-CoV-2 variant. Maybe COVID triggers immune dysfunction that leaves kids less able to fend off other viruses or keep them under control.

Important information for parents about hepatitis in

kids????????

Take home point: if your child shows signs of jaundice (yellowing of eyes / skin) see a doctor immediately!

Dr. Jerome Adams talks about mystery illness affecting children’s livers - WISH-TV https://t.co/l1faHnlNVk

— Jerome Adams (@JeromeAdamsMD) April 27, 2022

Good science takes time, and experts stress that it’s crucial to investigate all possible causes and not jump to conclusions prematurely. Investigators are interviewing parents, combing through medical records, testing for antibodies and analyzing liver biopsy samples in an effort to learn more.

While this investigation is underway, health officials are urging parents to be alert for hepatitis symptoms and asking clinicians to report suspected cases to their local or national health authorities.

Click here for more news about hepatitis.

Click here for more news about COVID-19.

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