

The Alabama Doc Who Sounded the Alarm on Unusual Hepatitis in Kids

— Markus Buchfellner, MD, and team were surprised by positive adenovirus results

by [Michael DePeau-Wilson](#), Enterprise & Investigative Writer, MedPage Today

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On a mid-October day in Birmingham, Alabama, Markus Buchfellner, MD, examined a young child admitted to Children's of Alabama with symptoms of vomiting, diarrhea and, most notably, a severe case of jaundice. It was the first in a series of mysterious cases that would lead to a CDC investigation.

"These kids just looked yellow; eyes, skin, everything," Buchfellner, a fellow in pediatric infectious diseases at the University of Alabama at Birmingham, told *MedPage Today*. "They looked like a jaundice newborn, and that is really concerning for liver disease."

For the first patient, Buchfellner's initial suspicions were confirmed by lab results that showed elevated levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin. After diagnosing the child with hepatitis, Buchfellner began testing for a wide array of possible causes. All of the testing was done at Children's, so the team included all possibilities, along with a few long shots, he noted.

The team tested for several viruses, including hepatitis viruses A, B, and C; Epstein-Barr virus (EBV); and even adenovirus. The patient tested negative for COVID-19 and had no prior documented case. Only the adenovirus test came back positive.

"We have the luxury of being able to get quick, rapid testing results back because we run most of our viral testing in house," Buchfellner said. "So, while adenovirus would have been unusual in this kid, we decided to send it since we were sending other viral testing."

The finding was surprising to Buchfellner and his team, in part because it was sent as an afterthought to the more expected differential diagnoses.

"We were actually a little bit concerned that it was a red herring, and that it wasn't real, perhaps that it could have even been a false positive because of how unusual the case was," he said.

Then, a couple of weeks later, a second case arrived.

"For me, two patients is a pattern," Buchfellner explained. "So, when the second case came in, and it seemed very similar to the first one, that's when I started to think that maybe there was something else here that we need to look into."

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At this point, Buchfellner reached out to the state health department and the CDC, which began investigation into the first two cases. The Children's team and representatives from the CDC sent sample packages for testing to the Wadsworth Center in Albany, New York.

Then more cases showed up -- every other week through the fall and into the winter, a new case with similar symptoms presented to Buchfellner and his team, for a total of nine patients.

According to the CDC's *Morbidity and Mortality Weekly Report* published in late April, testing revealed that several of the nine young patients had ALT and AST levels well over 1,000 U/L (ALT range 603-4,696 U/L; AST range 447-4,000 U/L). Eight of the nine patients also had elevated bilirubin levels. The patients' ages ranged from 1 year, 8 months to 5 years, 9 months.

The results for most of the testing were mixed. Six of the nine were positive for EBV, but none of the patients tested positive for hepatitis A, B, or C. Buchfellner and team were also able to rule out autoimmune hepatitis, as well as Wilson's disease and urinary tract infections in all of the cases. All nine patients tested negative for COVID-19 in the hospital, and none had a documented history of previous SARS-CoV-2 infection, although the team is currently planning to send further tests for potential antibodies.

Of note, all of the patients were healthy and on schedule for their standard childhood vaccines.

Of all the testing results, the most consistent finding was that of adenovirus. As Buchfellner and his colleagues documented in their report, "adenovirus was detected in whole blood specimens from all patients by real-time PCR testing."

However, the mystery did not end there for Buchfellner and his team.

"We've found adenovirus in the blood of nine patients so far with hepatitis, but we haven't been able to find the virus in the liver," he said. "The fact we weren't able to recover adenovirus in the liver means we need to do a little more investigation into this and we can't confidently say that there's a causation here."

The investigation into the nine cases in Alabama is ongoing. On May 6, the [CDC reported details](#) on over 100 more cases, as well as five deaths, with diagnoses very similar to the Alabama patients. Meanwhile, similar case clusters have emerged in other parts of the world, most notably in [England](#).

The cases continued coming into Children's until early February, when the last case was diagnosed, treated, and discharged. Since then, Buchfellner and the Children's team have been collaborating with the CDC to spread the word about these cases, in the hopes of preparing other hospitals for similar cases, and to gather more cases to study.

They are also planning to run further tests on the samples from the original nine patients, and hope to publish the findings later this year.

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