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INSIDE PEDIATRICS

CHILDREN'S, UAB AT EPICENTER OF CONGENITAL CMV RESEARCH

The city of Birmingham, home to the UAB Division of Pediatric Infectious Diseases at Children's of Alabama, will host the 7th International Congenital CMV Conference in 2019. Visit nationalcmv.org for updates. Nearly 35 years since inviting UAB researchers to study pediatric infectious diseases within its walls, Children's continues its mission of merging patient care and research under one roof.

"UAB and Children's have been the epicenter of congenital CMV research from the 1960s on, so we're talking 50 years of world leadership in research," said David Kimberlin, M.D., division co-director and the Sergio B. Stagno, M.D. Endowed Chair in Pediatric Infectious Diseases.

The division today includes eight physician-scientists and six PhDs. For researchers tasked with peeling back the layers of congenital CMV, the past is a prologue to the present and future. Currently, nine active NIH grants have been awarded to division members to conduct studies of CMV. In 2016, the National Institute of Allergy and Infectious Disease awarded \$11.5 million to support two studies, one of which will assess the treatment of babies born with congenital CMV but show no symptoms. About one out of every 200 babies in the U.S. is born with congenital CMV. However, only about one in five babies with congenital CMV will be sick from the virus, according to the Centers for Disease Control and Prevention, which has used division research results for its publications and recommendations.

The study will explore whether treating asymptomatic babies with four months of an oral drug – valganciclovir – will improve outcomes. The availability of reliable data about the natural history of congenital CMV suggested that a clinical trial with antiviral agents was feasible and could provide evidence that the outcome of congenital CMV could be modified by antiviral drugs.

Prior to valganciclovir, symptomatic babies or babies exhibiting symptoms of CMV were treated with the intravenous drug ganciclovir. As antiviral drugs became available in the 1980s, the late Charles A. Alford, M.D., the division's founder and first director, and Rich Whitley, M.D., current division co-director, approached the company that made ganciclovir and convinced the company to allow the drug to be studied for treating congenital CMV. When Kimberlin joined the division in the 1990s, he began work on an ongoing study spearheaded by Whitley and completed a phase 3 controlled study that determined ganciclovir improved outcomes when administered to symptomatic babies for six weeks. With the arrival of oral valganciclovir, a later study found six months of oral drug therapy for symptomatic babies improved audiologic and neurodevelopmental outcomes. The results were published in the *New England Journal of Medicine* in 2015.

"By showing long-term treatment in babies with symptomatic disease improves hearing and development, we definitively answered one question that had been raised three decades before – Does treating symptomatic congenital CMV work?" Kimberlin said. "In this new study of asymptomatic infants, we will treat for four months because our hypothesis is asymptomatic babies are not as sick, therefore, we can treat over a shorter time frame."

To identify asymptomatic babies for the new study, almost 50,000 babies will be screened at nine sites nationwide, including UAB/Children's. Once those babies are identified and enrolled, researchers will compare their findings to past data to determine the likelihood of asymptomatic babies developing hearing loss. Screening for the new study began in October 2017.

"If those incident rates overlap, then maybe treatment doesn't help very much at all. But if the incidents don't overlap, then it would suggest the treatment may be helping," Kimberlin said.



The UAB Division of Pediatric Infectious Diseases includes, standing, from left, Division Co-Director David Kimberlin, M.D.; Division Co-Director Rich Whitley, M.D.; Suresh Boppana, M.D.; Bob Pass, M.D.; and Scott James, M.D. Sitting, from left, Shannon Ross, M.D.; Sergio Stagno, M.D.; and Karen Fowler, PhD.