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Researchers find multiple tests needed to detect infection in low birth-weight newborns

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New research by Case Western Reserve University School of Dental Medicine and Yale University School of Medicine finds that cultures commonly used to detect bacterial infections in low birth-weight newborns with early onset sepsis may actually overlook some germs.

The research done at Case Western Reserve supports the need for multiple detection methods, such as DNA genomic analyses and other independent culture technologies, to identify bacteria that culturing may miss, said Yiping Han, professor of Periodontics and Reproductive Biology at the Case Western Reserve dental school and the corresponding author on the study.

An analysis of 44 prematurely-born babies, the majority of whom were diagnosed with early onset sepsis, was published in the journal PLOS ONE article, "Comparative microbial analysis of paired amniotic fluid and cord blood from pregnancies complicated by preterm birth and early-onset neonatal sepsis."

"Culture independent technology has broadened our scope of understanding human pathogens," said Han. The testing, under the lead investigator and Case Western Reserve postdoctoral scholar Xiaowei Wang, analyzed umbilical cord blood and amniotic fluid samples from Yale University medical school.

The researchers found more than 20 bacterial species not discovered using standard culturing. Some of the uncultured species appeared in

both the cord blood and amniotic fluid samples.

The uncultured bacteria were detected with DNA genomic analysis that Han's lab had used in a prior study that discovered the link between oral bacteria that causes still- or premature-births due to infected amniotic fluid that is supposed to be a sterile environment.

"By using molecular biology identity tools this is the first time we have shown that same microbes could move from the amniotic fluid into the fetal bloodstream," said Dr. Catalin S. Buhimschi, MD, from Yale University's Department of Obstetrics, Gynecology and Reproductive Sciences.

The bacteria enter the fetus' blood after the fetus ingests the amniotic fluid in the lungs or gastrointestinal tract.

Han said the discovery is further evidence of how oral bacteria travel into the maternal blood stream and eventually through the cord blood and amniotic fluid to the baby.

Researchers detected such uncultured bacteria as *Fusobacterium nucleatum*, which has a key-like mechanism that opens blood-vessel and cell walls to infect other areas of the body.

Han said DNA testing techniques were able for the first time to detect the oral bacteria— *Fusobacterium nucleatum*, *Begeyalla* and *Sneathia sanguinegens* —that brought on early neonatal sepsis and put newborns at risk of dying shortly after birth. Among these, *Fusobacterium nucleatum* was found at the same high frequency as the well-known *Escherichia coli*, putting the former on the same importance scale as the latter.

Early sepsis develops within 72 hours of birth. Its symptoms are varied, from apnea to low body temperatures. Four of every 1,000 births in the

U.S. develop the infections.

Baby's blood or spinal fluid is cultured for bacteria. A positive culture confirms sepsis, but many babies exhibit the symptoms of infection unconfirmed by culturing.

Standard management is to administer antibiotics for three days while doctors monitor the response to treatment.

Dr. Vineet Bhandari, MD, DM, associate professor of Pediatrics, Obstetrics, Gynecology, and Reproductive Sciences and director of the Program in Perinatal Research at the Yale University School of Medicine, raises concerns that widespread use of antibiotics could increase antibiotic-resistant bacteria when the exact bacteria are not targeted.

"This research is important in finding the right bug to target for antibiotics," Bhandari said.

Detecting bacteria is also more complicated if the mother has an infection prior to birth and is treated with antibiotics, the neonatologist said. Bhandari explained that treating the mother eliminates many cultured bacteria, making it difficult to determine what is infecting the baby.

Provided by Case Western Reserve University