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Gut microbes in healthy kids carry antibiotic resistance genes

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Friendly microbes in the intestinal tracts (guts) of healthy American children have numerous antibiotic resistance genes, according to results of a pilot study by scientists at Washington University School of Medicine in St. Louis. The genes are cause for concern because they can be shared with harmful microbes, interfering with the effectiveness of antibiotics in ways that can contribute to serious illness and, in some cases, death.

"From birth to age 5, children receive more antibiotics than during any other five-year time span in their lives," said senior author Gautam Dantas, PhD, assistant professor of pathology and immunology. "Frequent exposure to antibiotics accelerates the spread of antibiotic resistance. Our research highlights how important it is to only use these drugs when they are truly needed."

The results appear Nov. 13 in *PLOS ONE*.

With funding from the Children's Discovery Institute, the International Center for Advanced Renewable Energy and Sustainability, the National Academies Keck Futures Initiative and the National Institutes of Health (NIH), the researchers analyzed fecal samples from 22 infants and children ranging in age from six months to 19 years. The samples were provided by Phillip Tarr, MD, the Melvin E. Carnahan Professor of Pediatrics at Washington University School of Medicine.

Despite the small sample size, the analysis identified 2,500 new

antibiotic resistance genes, expanding the list of known antibiotic resistance genes by more than 30 percent.

"Microbes have been battling each other for millennia, regularly inventing new antibiotic synthesis genes to kill off rivals and new antibiotic resistance genes to defend themselves," Dantas said. "That microbial arms race is where this vast array of genetic resources comes from."

The scientists identified the new resistance genes by testing intestinal microbial DNA from the children against 18 antibiotics. The genes they identified impaired the effectiveness of all but four of the drugs. Many of the resistance genes were found clustered on sections of DNA that can easily jump from one microbe to another.

Babies lack microbes in their intestinal tracts at birth. Scientists have shown that infants establish their communities of gut microbes through ingestion of microorganisms from their environment – from crawling on the floor, for example, to putting toys and other objects into their mouths, to nursing and other contacts with their primary caregivers.

Dantas and his colleagues have been leaders in the development of functional metagenomics, in which scientists identify and analyze all the DNA from a microbial community. Instead of focusing either only on individual cultured organisms or computationally predicting functions from DNA sequences, researchers experimentally screen the DNA for specific functions, such as antibiotic resistance.

Dantas' primary research interest is the ecology and evolution of antibiotic resistance. According to a recent report by the Centers for Disease Control and Prevention, antibiotic-resistant infections cause at least 2 million illnesses and 23,000 deaths annually, adding $20 billion in health-care costs. Dantas noted that methicillin-resistant Staphylococcus

aureus, one of the most dangerous antibiotic-resistant bacteria, now causes more deaths in the United States than HIV. Scientists use the term resistome to refer to the collective antibiotic resistance genes of a microbial community.

"There were quite a few resistance genes in microbes from every child we looked at," Dantas said. "This was true even in children who were only six months old. When we compared their resistomes to those of older children, there didn't seem to be much difference."

Dantas' results, which must be confirmed through additional testing, suggest the resistome in the gut may become fixed more quickly than the distribution of species in the microbial community. The latter typically stabilizes three years after birth, but the study suggests the resistome may be set as early as six months after birth.

"This study gives us a snapshot of antibiotic resistance genes at single points in different children's lives," he said. "We're now analyzing the resistome's development via samples taken from the same children at multiple points in their lives."

More information: Moore AM, Patel S, Forsberg KJ, Wang B, Bentley G, Razia Y, Qin X, Tarr PI, Dantas G. Pediatric fecal microbiota harbor diverse and novel antibiotic resistance genes, *PLOS ONE*, online Nov. 13, 2013.

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