Study suggests early exposure to antibiotics may impact development, obesity

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Researchers at NYU School of Medicine have made a novel discovery that could have widespread clinical implications, potentially affecting everything from nutrient metabolism to obesity in children.

Since the 1950's, low dose antibiotics have been widely used as growth promoters in the agricultural industry. For decades, livestock growers have employed subtherapeutic antibiotic therapy (STAT), not to fight infection or disease, but to increase weight gain in cattle, swine, sheep, chickens and turkey, among other farm animals.

First author Ilseung Cho, MD, MS, and colleagues set out to reveal how antibiotics were acting on the body to create this effect, hypothesizing that low doses of the drugs may alter the composition and function of the bacteria in the gut. The resulting study, appearing August 22 online ahead of print in *Nature*, confirmed their theory about the gut microbiome, the term used to refer to the community of bacteria that lives in the stomach, and raises new questions about how manipulating it can impact metabolism and disease in the body.

The researchers administered STAT to normal mice and observed that the mice receiving antibiotics developed increased fat mass and percent body fat. After about six weeks, the mice that received antibiotics had gained about 10 to 15 percent more fat mass than the mice that did not receive antibiotics. The researchers also noted that bone density was significantly increased in STAT mice early in development and that particular hormones related to metabolism were affected by antibiotic

exposure, as well.

"By using antibiotics, we found we can actually manipulate the population of bacteria and alter how they metabolize certain nutrients," said Dr. Cho, assistant professor of medicine and associate program director for the Division of Gastroenterology at the School of Medicine. "Ultimately, we were able to affect body composition and development in young mice by changing their gut microbiome through this exposure."

Dr. Cho added that the scientific community is only now beginning to understand just how complex the microbiome is and how it affects health and disease. With a better understanding about the interactions between the microbiome and hosts and how these interactions can be manipulated, he and his colleagues believe the finding has the potential to affect a wide array of conditions ranging from childhood obesity to metabolic syndrome in adults.

Discovered in the early 20th century, antibiotics came into widespread use after World War II with substantial public health benefits. Use of these antibacterial agents has increased dramatically in the years since, now approximating one antibiotic course per year in the average child in the United States. However, there is increasing concern that antibiotic exposure may have long-term consequences, prompting a surge in recent research focused on the effects of antibiotics on development.

"This work shows the importance of the early life microbiome in conditions like obesity," said lead investigator Martin J. Blaser, MD, Frederick King Professor of Medicine and chair of the Department of Medicine at NYU Langone Medical Center. "The rise of obesity around the world is coincident with widespread antibiotic use, and our studies provide an experimental linkage. It is possible that early exposure to antibiotics primes children for obesity later in life."

Dr. Blaser advised that more research is needed to confirm this theory, but that manipulation of the gut microbiome may have implications for other conditions affected by the functions of bacteria in the gut. "We're still learning how far the impact of the microbiome reaches and the costs of perturbing it," he said.

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