Human microbiome influences rotavirus vaccine response

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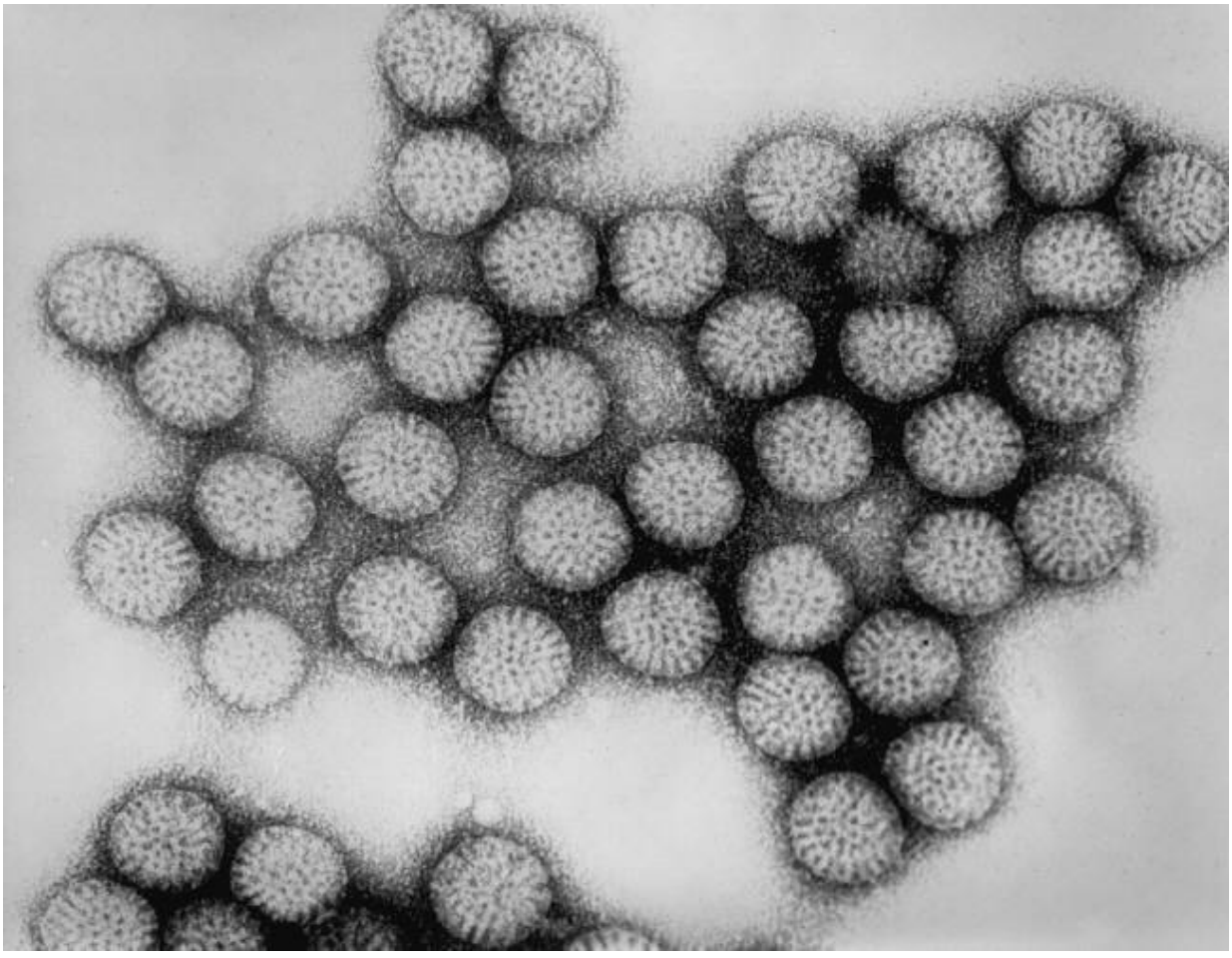

Transmission electron micrograph of intact rotavirus particles, double-shelled
Transmission electron micrograph of intact rotavirus particles, double-shelled. Credit: CDC

In a proof-of-concept study in healthy adult men, scientists in the Netherlands found that microbiome manipulation with antibiotics influenced the response to oral rotavirus vaccine. Specifically, they found higher levels of viral shedding in those receiving antibiotic treatment prior to vaccination compared with controls receiving no antibiotic treatment prior to vaccination. The study is a human demonstration that altering the bacterial intestinal microbiome can affect a vaccine's immunogenicity. The results appear August 8 in the journal *Cell Host & Microbe*.

"We found that the weakened live virus in the vaccine replicates at a higher level in antibiotic-treated recipients," says co- first author Vanessa Harris, of the Amsterdam Institute for Global Health and Development and the Division of Infectious Diseases and Center for Experimental and Molecular Medicine at the Amsterdam Medical Center, the Netherlands. "That means more virus was shed and we know from previous research that children who have higher shedding have better protection from the vaccine."

The researchers initiated the study to see if they could corroborate that the microbiome is related to vaccine performance. "If that is so, which we believe it is, then one could potentially use the microbiome to improve vaccine performance," says Harris, whose research has focused on the potential correlation between the microbiome and oral vaccine performance.

Rotavirus kills over 200,000 children each year and is the most important cause of diarrheal death in children. Previous research has shown that vaccines protect children against the disease but that they work less well in low-income settings. The reason for this was not well understood.

Working with co-first author Bastiaan Haak, Harris initiated the

63-person study to include healthy male adults randomized into two arms of antibiotic treatment: either broad spectrum with vancomycin/ciprofloxacin/metronidazole, where all bacteria were essentially killed, or narrow-spectrum with vancomycin. A no-vaccine control arm was also included. After antibiotic treatment and vaccination, subjects were assessed for antibody response and viral shedding. No differences were found in antibody levels between the three treatment arms except a slight increase in early vaccine boosting in the narrow-spectrum arm, but higher viral shedding was noted in the antibiotic-treated groups compared with the control arm.

In the team's earlier field work in children in Ghana and Pakistan, they found that infants with good immunity to the rotavirus vaccine had specific bacteria in their intestine. In this study, they added the vancomycin arm to see if they could replicate some of the microbiome findings found in those earlier field studies.

While the results from this study are limited since rotavirus is a childhood disease and the microbiome of infants and children is different in adults, the researchers are buoyed that their microbiome/vaccine response theory deserves further study.

"I think there is a fascinating interplay between the bacteria and viruses in our intestines and our intestinal immune system," says Harris. "All microbiota in the gut, including bacteria, fungi, and viruses, have evolved together for so long, it is very likely viruses exploit bacteria or immune responses in the gut to their advantage. Perhaps certain bacteria help the rotavirus replicate or antibiotics alter bacteria and thereby trigger immune responses that are favorable or unfavorable for a virus."

The team believes that understanding that triangulation between bacteria, virus, and the human immune system has potential for vaccinology and can lead to important uses of the microbiome that have not been realized

to date.

Harris emphasizes that this work does not advocate for antibiotic use in infants or children to boost rotavirus responses. Instead, the researchers view these results as a starting point with great potential for altering the microbiome to improve vaccine performance and ultimately better protect children in low-income settings from rotavirus, which continues to be a life-threatening disease.

More information: *Cell Host & Microbe*, Harris and Haak et al. "Effect of Antibiotic-Mediated Microbiome Modulation on Rotavirus Vaccine Immunogenicity: A Human, Randomized-Control Proof-of-Concept Trial." DOI: 10.1016/j.chom.2018.07.005 , www.cell.com/cell-host-microbe … 1931-3128(18)30375-5

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