

Source: Freedman SB, Williamson-Urquhart S, Farion KJ, et al. Multicenter trial of a combination probiotic for children with gastroenteritis. *New Engl J Med* 2018;379(21):2015–2026. DOI: 10.1056/NEJMoa1802597

Acute gastroenteritis accounts for approximately 1.7 million emergency department (ED) visits among children in the United States every year. Although health care providers traditionally have had little to offer to modify the disease course, probiotics are an expanding multi-billion-dollar industry with potential clinical benefits.

Consumers increasingly take probiotics to treat intestinal infections and 5–2 leading guidelines endorse the use of probiotics. Most studies of probiotics with results that have been published have had methodologic limitations and small sample sizes, have included limited investigations of causative pathogens, and have not reported adverse events. Numerous individual symptoms have been used as outcomes, but evaluations that incorporate both the duration and frequency of both diarrhea and vomiting are lacking.

The investigators in this trial involving children who had had symptoms of gastroenteritis for up to 72 hours and presented to the ED, a 5-day course of twice daily administration of a combined probiotic formulation (4.0×10^9 CFU of a combination *L. rhamnosus* and *L. helveticus*) did not prevent the development of moderate-to-severe gastroenteritis within 14 days after enrollment. Among these children with predominantly viral infection, probiotics did not result in benefits related to secondary outcomes. Adjustment for potential risk factors did not alter the findings.

Source: Brown JV, Meader N, Cleminson J, et al. C-Reactive protein for diagnosing late-onset infection in newborn infants. *Cochrane Database Syst Rev* 2019;1:CD012126. DOI: 10.1002/14651858.CD012126.pub2

Late-onset infection is the most common serious complication associated with hospital care for newborn infants. Because confirming the diagnosis by microbiological culture typically takes 24–48 hours, the serum level of the inflammatory marker C-reactive protein (CRP) measured as part of the initial investigation is used as an adjunctive rapid test to guide management in infants with suspected late-onset infection.

The authors conclude that the serum CRP level at initial evaluation of an infant with suspected late-onset infection is unlikely to be considered sufficiently accurate to aid early diagnosis or select infants to undergo further investigation or treatment with antimicrobial therapy or other interventions.

Source: Tomlinson MS, Lu K, Stewart JR, et al. Microorganisms in the placenta: links to early-life inflammation and neurodevelopment in children. *Clin Microbiol Rev* 2019;32(3):e00103–e00118. DOI: 10.1128/CMR.00103-18

Prenatal exposure to various stressors can influence both early and later life childhood health. Microbial infection of the intrauterine environment, specifically within the placenta, has been associated with deleterious birth outcomes, such as preterm birth, as well as adverse neurological outcomes later in life. The relationships among microorganisms in the placenta, placental function, and fetal development are not well understood. Microorganisms have been associated with perinatal inflammatory responses that have the potential for disrupting fetal brain development. Microbial presence has also been associated with epigenetic modifications in the placenta, as well other tissues.

In this review, they propose two processes, placental DNA methylation and inflammation, that could mediate a relationship between placental microbes and neurodevelopmental outcomes. From published studies of this relationship, some major themes emerge. The review also highlights a number of knowledge gaps in the understanding of the relationship between placental microorganisms and later life neurological outcomes.

Gaining a better understanding of which microorganisms in the placenta are associated with neurological disorders and the biological mechanisms driving this association could lead to improved identification, prevention, and treatment for these disorders.

Source: Gordillo Altamirano FL, Barr JJ. Phage therapy in the post antibiotic era. *Clin Microbiol Rev* 2019;32:e00066–e00118. DOI: 10.1128/CMR.00066-18

In this extensive review, the authors share a wide range of topics about phage therapy. The looming threat of antibiotic resistance calls for immediate action. Phage therapy is well suited to be part of the multidimensional strategies to fight against it. Simply put, phage therapy needs to be included in our repertoire of treatments against antibiotic-resistant pathogens, and the sooner the better. Additionally, there is no singular effective approach to clinical use of phage therapy, and in fact, its diversity and adaptability are among its greatest advantages.

Although some gaps in knowledge must be filled before we can standardize the use of phage therapy, the field is rapidly advancing. Finally, although the widespread use of phage therapy seems to be a challenging process, undertaking it will bring along societal, commercial, and economic benefits that will far outreach those from the clinical standpoint alone.

Source: Aliabadi N, Antoni S, Mwenda JM, et al. Global impact of rotavirus vaccine introduction on rotavirus hospitalizations among children under 5 years of age, 2008–2016: findings from the global rotavirus surveillance network. *Lancet Glob Health* 2019;7(7):e893–e903. DOI: 10.1016/S2214-109X(19)30207-4

Rotavirus vaccine use in national immunization programmes has led to declines in hospital admissions for rotavirus gastroenteritis among children; however, the global impact of rotavirus vaccine introduction has not been described using primary data. The authors describe the impact of rotavirus vaccine introduction on admissions for acute rotavirus gastroenteritis in primarily low-income and middle-income countries, using 9 years of data from the WHO coordinated global rotavirus surveillance network (GRSN).

The study reveals that, a significant and sustained reduction in the proportion of hospital admissions for acute gastroenteritis due to rotavirus was seen among children younger than 5 years in GRSN sites following rotavirus vaccine introduction. These findings highlight the need to incorporate rotavirus vaccines into immunization programmes in countries that have not yet introduced them and underline the importance of high-quality surveillance. The government of India will be introducing a rotaviral vaccine across the nation very soon.

Source: Bengtson AM, Sanfilippo AM, Hughes BL, et al. Maternal immunization to improve the health of HIV-exposed infants. *Lancet Infect Dis* 2018;19(4):e120–e131. DOI: 10.1016/S1473-3099(18)30545-0

The authors discuss various possibilities and scopes of maternal immunization in a woman with HIV positive status and its possible impacts on her infant. There is very little research that has explored the effect of HIV infection and HIV exposure on the immunogenicity and effectiveness of vaccines given during pregnancy, which is an important gap given the goal of passive immunity during the infant's first months of life.

For women living with HIV (WLWH) maternal immunization could be a promising strategy to reduce neonatal infections and improve maternal health. Maternal immunization could have important benefits for improving the health of HIV-infected women and reducing infectious disease-related morbidity and mortality in HIV-exposed but uninfected (HEU) children.

However, to maximize the benefits of maternal immunization for HIV-infected women and HEU infants, further research is required to investigate how HIV status influences the performance and clinical effect of vaccines administered during pregnancy.

