'Typhoid Mary' still stalks the world, but scientists show older vaccine works against the old foe

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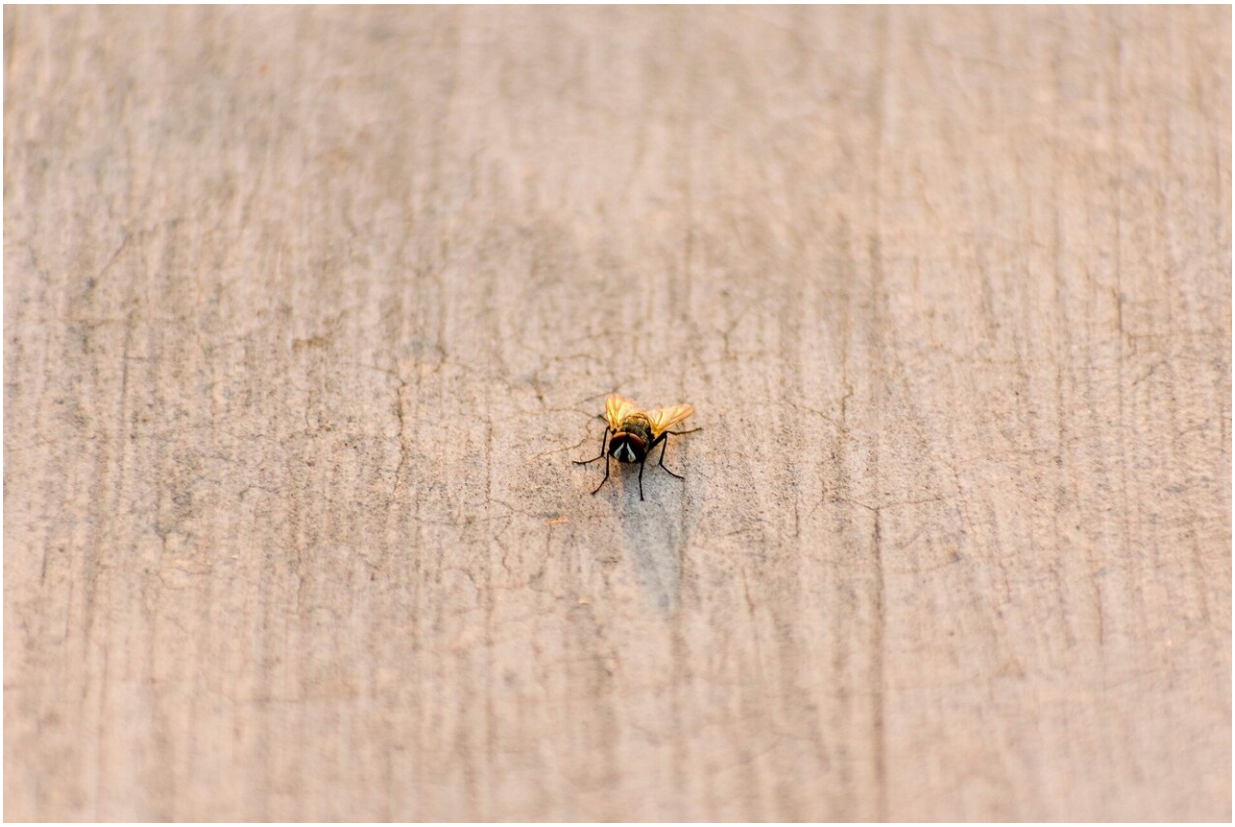

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Even as COVID-19 continues its rampage across the globe, an older health nemesis continues a more clandestine and increasingly deadly

spread.

Typhoid infects an estimated 11 million people a year and kills more than 160,000, largely in Asian and African countries with poor water and sanitation systems. Long treatable with antibiotics, the disease is growing resistant now, prompting health researchers to revive an older vaccine developed to prevent it.

In a study published in the *New England Journal of Medicine* last week, the researchers at the University of Maryland School of Medicine and elsewhere say their work shows the old vaccine can stop the infections. A single dose of the vaccine was more than 80% effective in preventing the disease in thousands of children in Malawi.

The evidence will provide heft to an effort already underway by an international group to distribute the vaccine in low- and middle-income countries.

"Typhoid is one of those diseases that causes fever and systemic illness in children and was readily treated with antibiotics," said Dr. Kathleen Neuzil, director of the university's Center for Vaccine Development and Global Health and a co-author of the study.

"The problem is that it's getting increasingly drug-resistant," she said. "So it's increasingly becoming severe and fatal again like before antibiotics were used."

Unlike COVID-19, which is caused by a virus, typhoid is caused by a kind of bacteria, Salmonella Typhi, which is different from the salmonella that causes stomach distress in the United States. Typhoid is spread through food and water contaminated with fecal matter.

While the disease is far more prevalent in Asia and Africa, there are

typically several hundred cases in the United States each year, mostly related to travel to developing countries. There were 21 reported in Maryland in 2019, according to the latest state data provided online.

For the study in Malawi, where typhoid is common, more than 14,000 children were given the vaccine by a group called TyVAC, or the Typhoid Vaccine Acceleration Consortium, which is based at the University of Maryland.

TyVAC is a partnership between the Neuzil's center, the Oxford Vaccine Group at the University of Oxford and the global nonprofit PATH, with the goal of accelerating use of so-called typhoid conjugate vaccines that are designed to produce a stronger immune response.

The group compared results from another 14,000 children in Malawi who didn't get the typhoid vaccine. They were given a vaccine for meningitis so they would still get an immediate benefit from participating in the trial.

Neuzil said there has long been another typhoid vaccine approved for use, but it's expensive and mostly used by travelers from wealthier countries, including the United States, each time they visit an affected country because the immunity it offers isn't long-lasting.

Also, that vaccine can't be used for those under age 2, excluding a large at-risk group of kids. Children also are routinely vaccinated against a number of diseases at one time at a young age and likely wouldn't return for an additional vaccine later.

The vaccine trial showed that protections from the old typhoid vaccine may last for years, maybe five or more.

Work on the vaccine began in 2001 in India by Barat Biotech

International, but the vaccine was not mass-produced before now for economic reasons, Neuzil said. Basically, poor countries couldn't afford it, while wealthier nations didn't need it.

It was given what's called prequalification by the World Health Organization in 2018 based on immune levels in recipients and good manufacturing procedures. There also have been limited other studies showing it works in different ages and geographic settings.

The large study from the field in Malawi could help secure buy-in from countries that have a lot of competing health concerns and may not have given typhoid priority at any age, Neuzil said.

Another international group, Gavi, an alliance funded with nonprofit and government money, agreed recently to pay for the vaccine and distribution for children as young as 9 months old during routine vaccination periods. The group also agreed to a one-time campaign to vaccinate older kids up to age 15.

Gavi also is working to distribute COVID-19 vaccine in low-income countries.

The vaccine study is promising, though the world still must live with typhoid for the foreseeable future, said Dr. Myron Levine, the Maryland medical school's associate dean for global health, vaccinology and infectious diseases.

Levine, co-founder of the Center for Vaccine Development and its former longtime director, has worked on typhoid prevention for decades and said the Malawi study provided important evidence of the vaccine's efficacy in an African country for the first time.

But even with widespread use of the vaccine—and improvements to

water systems—typhoid is sneaky. The bacteria-caused disease isn't passed on by animals but can be passed on by human carriers, sometimes known as a "Typhoid Mary." Tracking every one of them is nearly impossible in densely populated countries like Bangladesh and Pakistan where it's common.

However, it may be possible in a place like Samoa, Levine said. His work helped launch a vaccination and surveillance program in the tiny Pacific island years ago.

Still, he said, evidence of an effective long-lasting vaccine that can be used in small children comes at a good time, considering that only two antibiotics still seem to control the infections. Those treatments aren't always easy to come by and also could stop working.

"We are a step away from typhoid being untreatable, so if we don't prevent it, the fatality rate will really rise," he said. "This vaccine, it's really good news."