New low-cost method to deliver vaccine shows promise

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A health-care practitioner administers an intranasal vaccine. Credit: Content provider: CDC/Dr. Bill Atkinson Photo credit: James Gathany

Researchers have developed a promising new approach to vaccination for rotavirus, a common cause of severe diarrheal disease that is responsible for approximately 500,000 deaths among children in the developing world every year. In a study published in the November issue of *Clinical and Vaccine Immunology*, a vaccine delivered as nasal drops effectively induced an immune response in mice and protected them from rotavirus infection. The new vaccine delivery system has also been tested successfully and found to be heat stable with tetanus and is currently being tested with diphtheria and pertussis.

The team from the Cummings School of Veterinary Medicine at Tufts University and Tufts University School of Medicine collaborated with researchers from Boston and Tulane Universities to test the effectiveness
of immunization with harmless bacteria that were engineered to display rotavirus protein.

"The new vaccine, in conjunction with an agent that enhances immunity, induced sufficient antibody formation against rotavirus to protect mice against infection when the mice were exposed to rotavirus three weeks after their third immunization," explained John E. Herrmann, PhD, research professor in the infectious diseases division of the department of biomedical sciences at the Cummings School of Veterinary Medicine at Tufts University and the senior author of the published study.

"We created the rotavirus vaccine using a harmless bacterium called Bacillus subtilis (B. subtilis), which we can modify to display on its surface or in its cytoplasm proteins from infectious bacteria and viruses. When people are exposed to these proteins, they develop antibodies against them and therefore become immune to the bacteria and viruses," said the study's first author Sangun Lee, PhD, DVM, research associate at the Cummings School. "The B. subtilis bacteria are so harmless that they are part of the normal diet in several Asian countries."

"The vaccine with the Bacillus bacteria is very inexpensive to produce in large quantities and, unlike most traditional vaccines, requires no special purification steps before use. As a result, the cost of vaccine production is unusually low," explained Saul Tzipori, BVSc (DVM), DSc, PhD, Agnes Varis University Chair in Science and Society, distinguished professor of microbiology and infectious diseases, and director of the infectious diseases division of the department of biomedical sciences at the Cummings School. These findings are consistent with the team's previous studies in which they demonstrated that B. subtilis bacteria displaying a fragment of tetanus toxin protein completely protect mice from tetanus. Tetanus vaccines have been stored for more than a year at 113ºF without any loss of potency, a property that may be common to all B. subtilis vaccines."
Vaccines currently available have to be stored in refrigerators or freezers until the moment they are administered. This cold chain is difficult and costly to maintain. In many parts of the world, there is insufficient refrigeration or electricity to keep vaccines cold. The lack of refrigeration combined with the lack of trained personnel, especially in rural areas in developing countries, make it impossible for many children and adults to be vaccinated against standard infections, such as tetanus, rotavirus, diphtheria, \textit{pertussis} (whooping cough) and other diseases.

"In addition to being heat-stable and low-cost, the B. subtilis vaccines are given in the form of nasal drops or spray. A needle-free approach to vaccination is particularly advantageous in developing countries where clean needles and syringes and trained personnel are not always available," said team leader Abraham L. (Linc) Sonenshein, PhD, professor and acting chair of molecular biology and microbiology at TUSM and member of the genetics and microbiology program faculties at the Sackler School of Graduate Biomedical Sciences at Tufts.

"This vaccine project is still in the developmental stage," he continued. "The next major step for these vaccines is to show that they are safe and work well in humans, and then to extend the rotavirus and tetanus vaccine technology to include \textit{diphtheria}, \textit{pertussis} and other infectious diseases. Those diseases cause tens of thousands of deaths, particularly in newborns and in South-East Asia. We are actively looking for partners in the US and around the world to help us pursue our goal of reaching the point where many childhood and adult vaccines can be manufactured in a way that avoids the need for injection or refrigeration. Jerry Keusch of Boston University School of Public Health and I started this project 15 years ago and it has taken a long time to reach the stage where we now have effective needle-free vaccines. The technology has now advanced enough that we can expect to be successful with many other vaccines in a short time frame."

Provided by Tufts University


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