Vaccine against respiratory syncytial virus shows promise in early trial

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Credit: National Cancer Institute

Johns Hopkins Bloomberg School of Public Health researchers say a new candidate vaccine against respiratory syncytial virus (RSV) made with a weakened version of the virus shows great promise at fighting the disease, the leading cause of hospitalization for children under the age of one in the U.S.

There is currently no vaccine against RSV, which causes an estimated 66,000 to 199,000 deaths worldwide each year, and annual wintertime epidemics of respiratory illness in U.S. children.

Creating a vaccine with a live weakened virus - similar to what is used to prevent measles, mumps and rubella - requires a delicate balance: The virus must be weak enough so as not to make anyone sick and strong enough to induce a response from the body's immune system.

The researchers, who conducted a clinical trial that is reported in the Nov. 4 *Science Translational Medicine*, say they have used the virus' own machinery to create a vaccine that may protect young children from RSV disease. The vaccine, called MEDI ΔM2-2, is made from a genetically engineered version of the virus that is missing the gene for the M2-2 protein, a protein that acts like a switch. When M2-2 is deleted, the virus produces more of the viral proteins that trigger immune responses but less of the infectious virus that makes people ill.

"An RSV vaccine with this M2-2 deletion could tip the balance toward a better immune response, which is what we predicted based on earlier laboratory studies," says study leader Ruth A. Karron, MD, director of the Center for Immunization Research and a professor in the Department of International Health at the Bloomberg School. "From what we have seen in this small preliminary study in young children, this experimental vaccine is working as we hoped it would."

The vaccine, developed by the National Institutes of Health's Laboratory of Infectious Diseases at the National Institute of Allergy, Immunology and Infectious Diseases (NIAID), was sequentially evaluated in adults, older children who had previously been infected with RSV and infants and younger children who had not been exposed to the virus. The vaccine was given by nose drop, which allows development of immunity in the nose (where the virus initially takes hold) and throughout the

body.

The study showed that the vaccine being tested elicited more RSV antibodies in young children than a previous RSV vaccine candidate. The study also provided very preliminary evidence that some vaccinated children had strong 'booster' antibody responses when they encountered RSV in the community, but without RSV illness that required medical attention.

"These early clinical data are exciting, and make us think differently about the development of live vaccines for RSV," Karron says. "If this research is borne out in future studies, we could be less than a decade away from a safe and effective live-attenuated vaccine for RSV."

As the use of vaccines to prevent bacterial pneumonia in children have become more widespread, the importance of developing a vaccine for RSV has become even clearer.

"It's the next mountain to climb in terms of serious respiratory illness in children," Karron says.

More information: A gene deletion that up-regulates viral gene expression yields an attenuated RSV vaccine with improved antibody responses in children, *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.aac8463

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