

## Paving the way for respiratory syncytial virus prevention

Vaccine development against a widespread cause of respiratory illness in infants and young children

Respiratory syncytial virus (RSV) causes infections of the lower respiratory tract, mainly in infants and young children. Globally, the virus is responsible for over 30 million new acute lower respiratory infection episodes annually and up to 199,000 deaths in children under five years old, with 99 percent of these deaths occurring in low-resource countries.<sup>1</sup> It is so widespread in the United States that nearly all children become infected with the virus before their second birthdays.

Despite these impacts, no vaccine yet exists for RSV, leaving children vulnerable to infection and putting a heavy burden on caregivers and health care systems, particularly in the developing world where medical resources are limited and associated costs cause substantial economic hardship. The drug palivizumab—a monoclonal antibody that neutralizes the virus to provide protection—can help prevent RSV disease in high risk infants, but it cannot treat or cure RSV infection that is already serious. Furthermore, availability, cost, and treatment logistics make its use impractical in resource-constrained settings.

To most cost-effectively protect infants and children from this wide-reaching disease, particularly in the earliest months of life, developing a vaccine against RSV is critical. Through PATH's RSV vaccine project, we are investigating promising new vaccine technologies with the potential to help control RSV in the developing world through prevention. Because infants need the most immediate protection from RSV—with peak hospitalization rates occurring in children from birth to five months of age—the goal of this project is to advance the development of vaccines that can prevent serious RSV morbidity and mortality as early as possible in these youngest children.

Maternal immunization is one approach that holds promise for providing this kind of immediate protection for infants. Studies have shown that administering certain



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vaccines to pregnant women can help improve the mother-to-child transmission of antibodies, which can provide critical protection during the early stage of a newborn's life when direct vaccination is not an effective option. Due to RSV neutralizing antibody's correlation with protection against RSV, as demonstrated by palivizumab, the scientific community is exploring vaccines that induce neutralizing antibody and might be used in a maternal immunization strategy. We are partnering with vaccine developers and researchers from industry, academia, and other institutions to determine the feasibility of maternal immunization to protect children in the earliest months of life from this widespread disease.

## EXPLORING VACCINE OPTIONS AGAINST RSV

PATH is investigating potential clinical development partnerships with several companies and academic groups to advance the development of a RSV fusion (F) protein vaccine candidate. The ultimate goal is for the vaccine candidate to be administered to pregnant women so that high concentrations of maternal RSV antibodies can be transmitted to their offspring through the placenta before birth, providing protection against infection in the early infancy period when the disease burden is the highest. One potential candidate developed by Novavax, Inc. recently underwent a Phase 2 clinical trial in non-pregnant women of childbearing age in the United States with PATH support. Results from the study support progression to the next stage of clinical testing.

## RESEARCH TO SUPPORT RSV VACCINE DEVELOPMENT

PATH has established several research partnerships to advance the RSV vaccine field and provide information on the feasibility of a maternal immunization approach. We are collaborating with both Novartis Vaccines and Diagnostics, Inc. and GlaxoSmithKline Vaccines to develop RSV preclinical models for evaluating RSV vaccine candidates for pregnant women. These studies will include developing and optimizing *in vivo* and *in vitro* models designed to add to the RSV vaccine development toolbox. They will also inform on maternal immunization strategies going forward.

Current research suggests that vaccines designed to induce antibodies that neutralize RSV could prevent infection.

To improve the accuracy, reproducibility, and efficiency of measuring these essential neutralizing antibody responses, we are collaborating with the US National Institute of Allergy and Infectious Diseases (NIAID) through a team led by Dr. Barney Graham of NIAID's Vaccine Research Center to optimize a new platform for an RSV neutralization assay (or test). The format will enable scientists to uniformly and objectively assess neutralizing antibody as a measurable sign of protection. It will be an important step toward providing vaccine developers with a means to test and compare RSV vaccines.

Other research collaborations are evaluating the feasibility of RSV maternal immunization strategies in the developing world. In healthy populations, transfer of maternal protective antibody to the fetus is very efficient. In populations with chronic infections such as malaria or HIV, antibody transfer may not be as efficient. PATH is working with Dr. Ruth Karron at the Bloomberg School of Public Health, Johns Hopkins University; Dr. Christopher King at Case Western Reserve University; and Dr. Willie Pomat and colleagues at the Papua New Guinea Institute of Medical Research to assess how malaria present in the placenta affects the transfer of RSV-specific neutralizing antibody from mothers to infants. With Dr. Janet Englund of Seattle Children's Research Institute, PATH is studying RSV disease burden as well as the transfer and protective effect of maternal-derived RSV antibody in infants in Bangladesh and Nepal.

## Reference

1. Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. *The Lancet*. 2010;375(9725):1545-1555.



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