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With whooping cough cases on the rise, scientists develop and test new vaccines that aim to improve mucosal immunity.

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Improving Immunity with a Next-Generation Whooping Cough Vaccine

Keith Rubin from ILiAD Biotechnologies highlights current spikes in pertussis cases and discusses a new approach that outperforms traditional vaccines.

The Scientist Staff and ILiAD Biotechnologies

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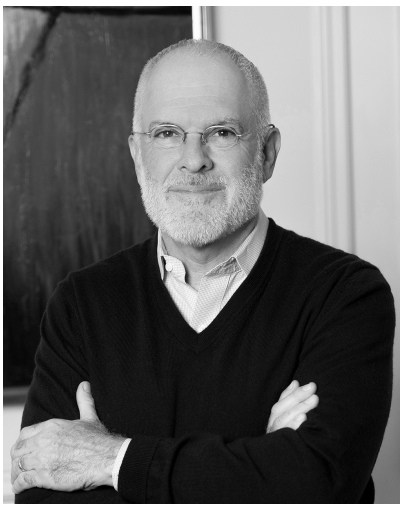
Whooping cough, also known as pertussis, has re-emerged worldwide and continues to be a major health concern. Caused by the bacterium *Bordetella pertussis*, this

contagious respiratory infection can cause severe disease and even death. The rise in cases is attributed to multiple factors, including reduced immunity in populations, in part due to declining vaccination rates and ineffective mucosal immunity provided by traditional acellular injectable vaccines.

In this Innovation Spotlight, Keith Rubin, the founder and CEO of ILiAD Biotechnologies, discusses the need for improved whooping cough vaccines and highlights promising clinical trials related to ILiAD's next-generation nasal spray vaccine.



What is the current situation concerning whooping cough cases and vaccination?

Despite high global vaccination rates with current vaccines, whooping cough remains a significant global health challenge with serious consequences, particularly for vulnerable populations such as infants and older adults. Outbreaks of whooping cough occurred worldwide in 2024 with 10-year highs in both the US and Europe.

Current injectable vaccines provide systemic immunity but have limited durability and are unable to prevent nasal bacterial colonization and transmission. This results from their inability to induce robust mucosal immunity in the upper respiratory tract where *B. pertussis* bacteria live and replicate and where pertussis disease begins.

What could be causing the spikes in whooping cough cases?

Recent whooping cough spikes are likely caused by multiple factors including rapidly waning immunity from acellular pertussis vaccines (aPVs) such as Tdap (tetanus-diphtheria-acellular pertussis), the inability of aPVs to prevent person-to-person transmission, and an increasing population of individuals who have only received aPVs during their lifetime (most individuals under age 27 in the US). Until there is a vaccine that induces potent mucosal immunity, reduces or prevents the reservoir of *B. pertussis* in the upper respiratory tract, and reduces or prevents transmission, the

cycle of pertussis epidemics is likely to continue.

How can a next-generation intranasal pertussis vaccine help control this disease?

Current injectable pertussis vaccines provide systemic immunity but are neither durable nor able to prevent bacterial colonization and transmission. The problem is that they do not induce robust mucosal immunity in the nose and nasal passages—precisely where whooping cough disease begins. This gap underscores the importance of developing an intranasal vaccine to elicit not only potent systemic immunity, but also strong nasal mucosal immune responses for the prevention of both nasal colonization and transmission. An intranasal vaccine that induces systemic immunity while at the same time halting both nasal colonization and transmission will be a decisive game-changer.

According to clinical trial data, a live attenuated nasal spray vaccine for whooping cough may provide better protection compared to injectable vaccines.

TELEFLEX MEDICAL INC.

BPZE1 is the leading next-generation pertussis vaccine designed to induce comprehensive and durable protection against *B. pertussis* infection (colonization) and disease (whooping cough). BPZE1 is a live attenuated intranasal spray being developed to block *B. pertussis* from colonizing and infecting the nasal passages of adults and children, to protect adults and children from whooping cough, and to potentially prevent transmission, including transmission to vulnerable infants. BPZE1 is designed to safely and effectively mimic the excellent systemic and mucosal immunity induced by natural pertussis disease without the symptoms.

How has BPZE1 performed in clinical trials compared to currently available vaccines for whooping cough?

To date, ILiAD has completed six clinical trials, including four phase 2 studies. For example, a phase 2b controlled human infection model (CHIM) BPZE1 study

completed in 2023, conducted in 53 adult participants in the United Kingdom, is the first and only human study to demonstrate vaccine protection against virulent *B. pertussis* challenge. In this study, BPZE1 was able to demonstrate protection from colonization post-challenge compared to a placebo control group. In an earlier phase 2 study published in *The Lancet*, BPZE1 protected 90 percent of study participants from colonization by a challenge strain of attenuated *B. pertussis*, while the majority of Tdap-vaccinated individuals were colonized post-challenge.[1]

Following discussions with regulatory agencies, we are now planning for the initiation of the pivotal phase 3 controlled human infection model (CHIM) study that will support global marketing applications by conducting a head-to-head study of BPZE1 versus a current Tdap vaccine.

BPZE1 also demonstrated positive interim results in our SUPER (*Stand Up to Pertussis*) school-age trial conducted in 366 participants in the United Kingdom, Australia, and Costa Rica. The recently completed SUPER trial is the first study of BPZE1 in healthy children six to 17 years of age. In this study, a single intranasal dose of BPZE1 with and without co-administration of tetanus, diphtheria, and acellular pertussis vaccine (Tdap, Boostrix®) induced mucosal antibody responses. In addition, when given in combination with Tdap, BPZE1 induced systemic immunoglobulin G (IgG) responses equal to or greater than responses induced by Tdap alone.

In both pediatric and adult trials, a favorable safety profile has been established for BPZE1.

What is on the horizon for this next-generation whooping cough vaccine?

Our BPZE1 live attenuated intranasal vaccine is currently in development as a booster for children ages six to 17 years of age, and adults 18 years of age and older. BPZE1 has demonstrated the unique ability to induce both systemic and nasal mucosal immune responses which offer the potential to protect against pertussis disease (whooping cough), infection (colonization), and transmission. Having completed six clinical BPZE1 trials, we are now planning for the initiation of the

pivotal phase 3 CHIM study to support global marketing applications.

Reference

1. Keech C, et al. Immunogenicity and safety of BPZE1, an intranasal live attenuated pertussis vaccine, versus tetanus–diphtheria–acellular pertussis vaccine: a randomised, double-blind, phase 2b trial. *The Lancet*. 2023;401(10379):843-855.

INNOVATION SPOTLIGHT