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Successful test in humans of a nasal vaccine against pertussis

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The CHILD-INNOVAC European research programme, coordinated by Inserm, has enabled the development of an innovative vaccine that can be administered intranasally, to combat pertussis, which has shown a resurgence in developed countries in recent years. The research consortium, headed by Camille Locht, Director of the Centre for Infection and Immunity of Lille (a joint Unit involving Inserm, CNRS, Institut Pasteur de Lille and University of Lille Nord de France), today published promising results from Phase I clinical trials of the vaccine in human subjects in the online journal *PLOS ONE*.

Researchers from the CHILD-INNOVAC European project, which brought together 10 European partners*, evaluated the efficacy and safety of a new concept in intranasal vaccination against pertussis. They also carried out clinical trials in humans, which provided conclusive results.

Pertussis is a wrongly "forgotten" disease, according to Camille Locht, a Research Director at Inserm and Director of Scientific Affairs of the Institut Pasteur de Lille. The disease currently affects several tens of millions of individuals, and kills approximately 300,000 children annually worldwide. The associated morbidity and mortality are increasing throughout the world. Its resurgence has become a matter for major concern since 2010 in some developed countries, such as the USA, Australia, the UK, the Netherlands and France.

The CHILD-INNOVAC project is more specifically focused on

combating two major respiratory pathogens: Bordetella pertussis (the bacterium that causes whooping cough) and respiratory syncytial virus (which causes bronchiolitis in infants). These pathogens mainly affect infants aged 0 to 6 months, who are poorly protected by the vaccines presently available. The project also provides proof of concept that this vaccine may be applied to other respiratory infections.

The researchers from the CHILD-INNOVAC project have succeeded in testing in humans, for the first time, a live bacterial vaccine, genetically attenuated and specially designed for intranasal administration to combat major respiratory pathogens. "This original method of administration will make the vaccine accessible to greater numbers of people at a smaller cost," explains the project coordinator, Camille Locht.

The Phase I trials in humans allowed the immunogenicity and safety of the vaccine to be measured in comparison with a placebo, under double-blind conditions. They took place in Sweden, which has the most "naive" population with respect to vaccination against pertussis, given that vaccination was abandoned in that country for several years, for reasons of inefficacy.

The main objective of these trials was to record all possible adverse events, namely cough, sneezing, nasal discharge, effects on general health, etc. These measurements were examined by an independent data monitoring committee.

The second objective was to assess colonisation of the nasal mucosa by the vaccine, and the triggering of an immune response.

It was possible to test three different doses of the vaccines: a low, intermediate and high dose. Results obtained after monitoring the vaccinated subjects for 6 months, and analysing 60,000 data points, showed that the vaccine induced no adverse events compared with the

placebo, even at the high dose. The vaccine colonised the nasal mucosa best at the high dose. Moreover, immune responses were triggered in all subjects whom the vaccine had colonised. "It is of special interest that a single nasal administration was able to induce an immune response that was maintained for at least 6 months, i.e. for the duration of the study," comments Camille Locht.

The next step will involve administering higher volumes in an effort to increase the level of colonisation of the nasal mucosa by the vaccine. Camille Locht and his collaborators also hope to improve the stability of vaccine over time, with a view to industrial development in the near future.

Inserm Transfert, in charge of the valorization of the IP portfolio related to the BPZE-based technology, recently entered into an agreement with a biotech partner to further develop the technology.

More information: dx.plos.org/10.1371/journal.pone.0083449

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