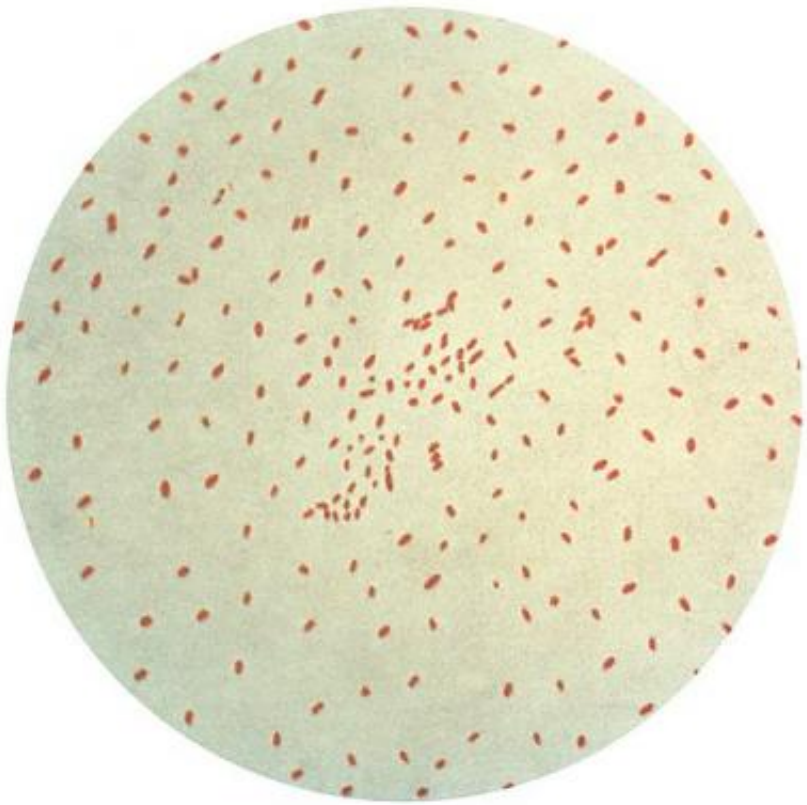
Decades-long trends, not flawed vaccine, explain resurgent whooping cough

March 28 2018



Gram stain of the bacteria Bordetella pertussis. Credit: CDC

Researchers and public health officials have struggled to explain the

resurgence of whooping cough in the United States since the late 1970s, and the suspected shortcomings of the current generation of vaccines are often blamed.

But a new University of Michigan-led study concludes that the resurgence of the highly contagious respiratory disease is the result of factors—including a phenomenon known as the honeymoon period—that began in the middle of the last century, long before the latest vaccines were introduced in the late 1990s.

"Conventional wisdom is that the current vaccine is the problem, but that's not consistent with what we see," said Aaron King, a U-M infectious disease ecologist and applied mathematician.

King and colleagues from the Institut Pasteur, the University of Georgia and Queens University concluded that natural population turnover, incomplete vaccination coverage, and slowly waning protection from a highly effective yet imperfect vaccine best explain the resurgence of whooping cough. The disease can be fatal to infants and is also known as pertussis.

"This resurgence is the predictable consequence of rolling out a vaccine that isn't quite perfect and not hitting everybody in the population with that vaccine," said King, a professor in the U-M Department of Ecology and Evolutionary Biology and in the mathematics department.

The team's findings are scheduled for publication March 28 in *Science Translational Medicine*. The first author of the paper is Matthieu Domenech de Cellès, formerly a U-M postdoctoral researcher under King, now at the Institut Pasteur in Paris.

"Our results are important because they show that recent trends in pertussis are not necessarily caused by recent changes in epidemiology or

biology," said Domenech de Cellès.

"Rather, the contemporary epidemiology of pertussis may be interpreted as a legacy of longstanding immunization practices. It's an important shift of perspective, which makes pertussis a complex but exciting system to study."

The researchers used disease-transmission models and 16 years of age-stratified pertussis incidence data from Massachusetts, along with statistical methods for extracting information from the data. The authors say their results apply to the rest of the United States and to Western Europe.

According to the study, the introduction of the first pertussis vaccine in the late 1940s led to a honeymoon period, a time of very low disease incidence following the start of a vaccination program. The return of pertussis in recent decades signals the end of that honeymoon period, according to the researchers.

In the pre-vaccine era, whooping cough was a very common childhood disease in the United States. Most kids were exposed to Bordetella pertussis, the bacterium that causes it, and their immune systems mounted a strong response that provided long-lasting immunity. As a result of those naturally acquired infections, most adult Americans were immune to pertussis.

Routine vaccination with a whole-cell pertussis vaccine quickly led to a 100-fold reduction in incidence. Actually, two factors accounted for that sharp drop-off: children protected by the new vaccine and adults with natural immunity acquired in the pre-vaccine era.

But as the decades passed, the number of American adults with naturally acquired pertussis immunity gradually declined as that older group died

out.

Concurrently, the number of pertussis-susceptible U.S. adults was on the rise, setting the stage for the resurgence. The susceptible adults included people who were not vaccinated as children and who also avoided naturally acquired pertussis infections.

The mathematical model that best fit the 1990-2005 Massachusetts incidence data was one that explains the current resurgence "as a legacy of incomplete vaccination with effective, but imperfect, vaccines against a background of slow demographic turnover, i.e., as an end-of-honeymoon effect," the authors wrote.

The modeling study also supports the idea that protection from the pertussis vaccine gradually wanes over time—though it lasts a lot longer than many experts believed.

Some critics of the current acellular pertussis vaccine say it wears off after five to seven years. But the new study "suggests that current pertussis vaccines provide lifelong protection to 55 percent of people and protect 90 percent of people for more than a decade," said study co-author Pejman Rohani, a population ecologist at the University of Georgia's Odum School of Ecology."Furthermore, our models explain that patterns of pertussis incidence previously attributed to rapid vaccine waning are actually consistent with higher contact rates once children enter school."

Though the current vaccine is effective at reducing levels of the pertussis pathogen circulating in the population, routine vaccination alone will never be sufficient to eradicate the bacterium, the researchers conclude.

In infants, pertussis causes violent, gasping coughing spells and can lead to life-threatening complications. People with whooping cough usually

spread the disease by coughing or sneezing while in close contact with others. Parents, older siblings or other caregivers can give whooping cough to babies without even knowing they have the disease.

The modeling study identified primary school children and teenagers as the "core transmission group" mainly responsible for spreading the disease. In one simulation, a booster vaccination effort focused on children ages 5 to 10 or 10 to 20 led to a drop in infant cases of about 25 percent.

"The overwhelming amount of transmission is happening in those age groups," King said. "So, we have to make sure that kids are getting vaccinated before they go to school. That's going to have the biggest impact."

The U.S. Centers for Disease Control and Prevention recommends a series of five pertussis shots for children under 7. Additional shots are recommended for older children and for some adults.

Pertussis is responsible for 195,000 infant deaths each year worldwide, mostly in the developing world. There were 17,972 reported pertussis cases in the United States in 2016, including six infant deaths, according to the CDC.

More information: M. Domenech de Cellès el al., "The impact of past vaccination coverage and immunity on pertussis resurgence," *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aaj1748

Provided by University of Michigan