

Implications of Secular Patterns in Reported Pertussis in the United States. John Glasser, Charles LeBaron, Phil Smith, Ben Schwartz<sup>1</sup>; Stephanie Schauer, Susan Lett<sup>2</sup>; and Patrick Olin<sup>3</sup>. Centers for Disease Control and Prevention<sup>1</sup>; Massachusetts Department of Public Health<sup>2</sup>; Swedish Institute for Infectious Disease Control<sup>3</sup>

In the United States, pertussis seems to be increasing among adolescents, middle-aged adults, and infants aged <4 months, for whom it may be fatal. A multi-state study implicates parents, and to lesser extent grandparents and siblings, as sources of infant infection. The increase among adolescents and middle-aged adults coincides with a decrease among children in Massachusetts. *Methods:* We modeled pertussis via realistic systems of differential equations to evaluate a hypothetical cause of these secular patterns, diminished boosting of shorter-duration, artificially induced immunity as vaccination has reduced childhood disease, and its remedy by re-vaccination. We estimated initial conditions from IgG titers to pertussis toxin (PT) in sera from southerners who participated in an unrelated vaccine trial. And we adjusted age-specific infection rates, obtained from pre-vaccination disease histories, to minimize disparities between predictions and reports to the National Notifiable Diseases Surveillance System (NNDSS). Because disease peaks among adolescents in fall and other age groups in summer, and policymakers are considering adolescent re-vaccination, we simultaneously estimated coefficients of age-specific seasonal forcing. *Results:* In the US, risks per susceptible (forces of infection, FOI) calculated from these adjusted rates peak at successively lower levels during childhood, adolescence and middle age, as does IgG to PT from sera obtained in conjunction with the 1991-'94 National Health and Nutrition Examination Survey (NHANES III). In MA, the FOI on adolescents apparently exceeds that on children. And, compared with reports to the NNDSS, our MA model predicts proportionately fewer cases among persons 15-19 years old, and more aged 20-24, while our US model's predictions are concordant ( $p < 0.01$  via Kolmogorov-Smirnov). *Conclusions:* 1) Increasing diagnostic suspicion, evolution of *Bordetella pertussis* in response to vaccination or deterioration of vaccine potency are not required to explain observed secular patterns, but neither are these alternative hypothesis mutually-exclusive. 2) Nonetheless, the discrepant MA model predictions, disparate age-specific FOI and regional analyses of sera from NHANES III corroborate our explanation: relatively few children in MA are susceptible by virtue of sustained vaccine coverage at higher levels than yet attained throughout most of the US, which is why childhood disease is scarce. And relatively more adolescents and middle-aged adults are susceptible by virtue of the waning of artificially induced immunity, which is why adolescent and middle-aged adult pertussis is increasing. *Implications:* Re-vaccination of adolescents, and possibly selected middle-aged adults, could not only reduce disease in MA, but also ensure that adults caring for infants (i.e., 20-24 and 30-49 year olds contribute most to their FOI in our US model) were immune or subject to reduced FOI. Simulations confirm these deductions, with late adolescent vaccination optimal. *Predictions:* In Sweden, where 3-dose coverage exceeded 98% soon after resumption of vaccination following a 17-year hiatus, boosting via exposure must have declined abruptly as immunity began shifting from longer-duration, naturally acquired to shorter-duration, artificially induced. Absent adolescent re-vaccination, disease among young infants will increase as parental immunity wanes.