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Session: Enteric Fever: The Accelerated Agenda to Deliver Conjugate Vaccines

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Room: Room 1.60

The rapidly re-emerging burden of endemic typhoid fever in the 21st Century: A preventable by-product of massive urbanization in the developing world?

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Sub-Saharan Africa is urbanizing at a rate of 3-5% with > 70% of new urban residents settling in informal settlements, which are urban slums with high population density and limited sanitation, hygiene and water quality. Likewise, municipalities in south and southeast Asia are dominated by similar informal settlements. As a result, water-borne and food-borne diseases are frequently seen. Typhoid fever, a rare entity in wealthy nations, is highly endemic in urban slums in Kenya, Bangladesh, India, Pakistan and Indonesia. Adjusted incidence rates are highest in children 2-to-10 years of age and have been documented to be as high as 2 per 100 person-years in Nairobi, Kenya, and are likely as high or higher in many other settings with similar conditions. Among available interventions to reduce the immense burden of typhoid fever, typhoid vaccines appear to be most likely to have the greatest effect at least for the foreseeable future. Existing Vi capsular polysaccharide vaccine induces T-cell independent antibody responses; thus, repeat vaccination would not produce a booster effect and the vaccine would not be useful in children <2 years of age. While mass vaccination campaigns in children > 2 years old and adults could be considered in highly endemic areas, the vaccine could not be incorporated into existing routine infant immunization programs; in addition, efficacy in south Asian slum settings has been variable and relatively low (61% in Kolkata and <50% in Karachi). New protein conjugate vaccines hold promise, as do new oral live-attenuated typhoid vaccines which will be available in liquid format and appear to be immunogenic with a single dose. Hand hygiene, availability of toilets and sewage management, as well as water treatment would likely have substantial additional impact. Endemic typhoid is a marker for insufficient infrastructure and for inequities in formal government services. Ultimate solutions rest with raising minimum standards of living in urban environments and may require innovation, investment, and commitment from business and technology sectors, local and national governments, academia, and society.

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Modeling the potential impact of typhoid conjugate vaccinesV.E. Pitzer^{1,*}, C.C. Bowles², S. Baker³, B.T. Grenfell⁴¹ Yale School of Public Health, New Haven, CT, USA² Harvard School of Public Health, Boston, MA, USA³ Oxford University Clinical Research Unit - Hospital for Tropical Diseases, Ho Chi Minh, Viet Nam⁴ Princeton University, Princeton, NJ, USA

Mathematical modeling of the transmission dynamics of *Salmonella* Typhi allows for an evaluation of the potential impact of vaccination and a quantification of the expected direct and indirect effects of vaccines under a variety of scenarios regarding vaccine efficacy and program implementation. We developed an age-structured compartmental model that reflects the natural history and immune response to infection with *Salmonella* Typhi. We fit our model to data on culture-confirmed cases of typhoid fever from a variety of settings in South Asia in order to estimate important model parameters, such as the basic reproductive number (R_0). We then evaluated the potential impact of routine vaccination and/or vaccination campaigns targeted at different age groups. We parameterized the vaccine efficacy and duration of protection based on data for Vi-polysaccharide and Vi-conjugate vaccines. Our model was able to reproduce the incidence pattern and age distribution of typhoid cases in Vellore, India; Kathmandu, Nepal; and Dhaka, Bangladesh for different values of R_0 in these settings. Vaccination was predicted to confer substantial indirect protection in the short term, leading to a decrease in the incidence of typhoid. However, waning of vaccine-induced immunity could lead to a rebound in typhoid incidence 5-15 years after vaccine introduction. Model predictions for the overall and indirect effects of typhoid vaccination and prospects for elimination depend strongly on the role of chronic carriers in transmission. Elucidating the role of chronic carriers in transmission in different settings is a pivotal area for future epidemiological research. Our results suggest that is unlikely that typhoid can be eliminated from high incidence endemic settings through vaccination alone.

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