CORRESPONDENCE

Field Effectiveness of Vi Polysaccharide Typhoid Vaccine in the People’s Republic of China

To the Editor—Field investigations in the People’s Republic of China to determine the protective efficacy of typhoid Vi polysaccharide vaccine (Vi vaccine) were done among students attending a middle school [1]. Vi vaccine was offered to students even during an outbreak of typhoid fever. The efficacy was 73% among those immunized before the outbreak and 71% among vaccine recipients during the outbreak. Many vaccine failures during the vaccine efficacy trials might have been caused by infection with Salmonella serotype Typhi strains that were lacking the Vi antigen. Vi-negative Salmonella Typhi cause a disease indistinguishable from that caused by a Vi-positive strain [2]. On their entry to an intracellular niche, Vi-negative Salmonella Typhi are protected from the Vi antibody [3]. Since Vi vaccines would not elicit any cellular immunity, they would not stop intracellular replication of Salmonella Typhi.

Vi-negative Salmonella Typhi selected during a slide agglutination test with Vi typing antisera have been known for several decades. Salmonella Typhi isolates that lacked the ViaB genetic sequences were responsible for an epidemic of multi-drug-resistant typhoid fever in Calcutta, India [4]. The role of Vi-negative Salmonella Typhi infections in the People’s Republic of China should be determined immediately, and bacterial field isolates should be characterized fully in a reference laboratory.

A high molarity affects the expression of the Vi antigen, rendering an otherwise Vi-positive isolate into an apparently negative one. Genotyping investigations for ViaB sequences on isolates would indicate the role of Vi-negative Salmonella Typhi in any failures with Vi vaccine, in locally produced batches of vaccine [1] and in the conjugated Vi vaccine bound to nontoxic recombinant Pseudomonas aeruginosa exotoxin A [5].

Establishment of ViaB genotyping facilities in the People’s Republic of China would be cost effective, and characterization of Salmonella Typhi isolates would be an asset to antityphoid strategies. Genotyping would indicate the contribution of Vi-negative Salmonella Typhi in partial failures [1, 5] of Vi vaccines.

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References

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Reply

To the Editor—Dr. Arya [1] raises the point that Vi vaccine failures might be related in part to infections by Salmonella serotype Typhi that do not express the Vi capsular antigen. We are unable to comment on this possibility in relation to the outbreak among schoolchildren in the People’s Republic of China, which provided us with the opportunity to assess the effectiveness of Vi vaccine in the field [2]. However, several observations suggest that Vi-negative clinical isolates do not provide a plausible explanation for the majority of Vi vaccine failures.

First, it is well documented that Salmonella Typhi clinical isolates may lose expression of Vi capsule with repeated replication in vitro. This can lead to false-negative assessments about the presence of the Vi capsule unless fresh clinical isolates are tested. In a recent large-scale population-based study of typhoid fever in urban Delhi, the possibility of Vi-negative isolates was explicitly addressed by testing fresh Salmonella Typhi isolates from blood cultures for the presence of Vi capsular antigens with slide agglutination [3]. Of 93 isolates tested, 92 expressed Vi capsular antigen (M. K. Bhan, personal communication). Second, in a recent trial of Vi polysaccharide-protein conjugate vaccine in Vietnamese children, vaccine efficacy was 92%, which is higher than levels found for Vi polysaccharide vaccine in other studies, suggesting that Vi vaccine failures might be related more to lower-than-protective serum anti-Vi antibody responses than to Vi-negative S. typhi [4]. Nevertheless, we agree that Dr. Arya’s observations about Salmonella Typhi lacking ViaB genetic sequences are of interest and deserve further evaluation in other typhoid-endemic settings.

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