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Molecular Analysis of Isolates of *Salmonella typhi* from Patients with Fatal or Nonfatal Typhoid Fever or Aberrant Clinical Presentations

Thong et al. (6) reported on the results of pulsed-field gel electrophoresis (PFGE) of 52 isolates of *Salmonella typhi* from Papua New Guinea using chromosomal DNA digested with three restriction endonucleases. These isolates were reported susceptible to the 16 antibiotics tested and were devoid of plasmids (6). The PFGE pattern combination of X1S1A1 was manifest in all isolates from patients with fatal typhoid fever, while patients with nonfatal infections exhibited different pattern combinations. Genetic diversity was apparent in blood and fecal isolates of *S. typhi* from the same patient. The utility of PFGE in epidemiological and therapeutic interventions against *S. typhi* infections in the individuals or community would be more apparent had PFGE analysis been carried out on multidrug-resistant strains of *S. typhi* from Papua New Guinea, if any, as well as on isolates from other geographical locations.

It would also be of interest to have PFGE profiles of isolates from those coinfected with human immunodeficiency virus (HIV). In regions in developing countries in which typhoid fever is endemic, such coinfection is associated with an aberrant clinical picture, including fulminant diarrhea (2). Even in locations in industrialized countries in which typhoid fever is not endemic, all those coinfected with HIV run an increased risk of typhoid and paratyphoid infections (5). Furthermore, PFGE patterns of isolates recovered from patients with atypical clinical presentations would be of interest.

The recent reports of hydronephrosis from a typhoid abscess (1), cholestatic jaundice (4), central nervous system involvement (7), and common iliac artery occlusion (3) have indeed been astounding.

In summary, comprehensive PFGE data on *S. typhi* strains from such unusual clinical cases, on strains exhibiting plasmids, and on strains with multidrug resistance as well as on those from patients presenting with a fulminant picture due to coinfection with HIV would help establish both qualitative and quantitative polymorphism characteristics that might be linked to virulence. Knowledge of such virulence associations might allow us to classify certain PFGE characteristics as predictive of novel emerging disease patterns, a fulminant or fatal outcome, or a less severe course of infection.

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Author's Reply

My coauthors and I thank Dr. Arya for his comments related to our article on the molecular characterization by PFGE of *S. typhi* isolates from patients with fatal and nonfatal cases of typhoid fever (2). We would agree with Dr. Arya that, in order to further vindicate the value of PFGE, it would be of interest to analyze multidrug-resistant strains of *S. typhi* by this method. Unfortunately, our studies to data have been performed with *S. typhi* strains from regions (e.g., Malaysia, Indonesia, and Papua New Guinea) where these resistant strains are still relatively uncommon in contrast to the situation on the Indian subcontinent. In addition, the presence of plasmids, especially high-molecular-weight ones commonly associated with antibiotic resistance in *S. typhi*, can complicate the interpretation of PFGE patterns due to the presence of plasmid or plasmid-derived DNA fragments. We fully agree with Dr. Arya that it would be most interesting to perform molecular analysis of *S. typhi* strains from HIV-infected individuals and AIDS patients, especially those isolates obtained from patients with atypical presentations and those causing fulminant disease. We would be most interested in collaborating with colleagues in possession of such strains. These molecular approaches, together with recent information on major genomic rearrangements in the *S. typhi* genome (1), may ultimately provide important information on the molecular basis of virulence of this important human pathogen.

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