Investigating the Mucosal Antibody Response in Typhoid and Paratyphoid Fever

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Background: Design of diagnostic tools and efficacious vaccines against enteric fever is hampered by our limited understanding of localisation of the pathogen in the body and of the balance of mucosal and systemic responses preceding and following clinical manifestation of infection. We hypothesised that clinical symptoms of enteric fever may be linked to the level of intestinal mucosal response specific to *Salmonella* antigens and investigated this in a controlled human infection model (CHIM).

Methods: Using an established enteric fever CHIM in a non-endemic setting, we compared serum and copro-antibody responses from healthy volunteers within two groups: immunologically naïve volunteers with no prior exposure to *Salmonella* Typhi or *Salmonella* Paratyphi; and volunteers previously-exposed to *Salmonella* Typhi or *Salmonella* Paratyphi in earlier challenge studies. Antigen-specific (O9:LPS or O2:LPS) IgA and total IgA ELISA assays were undertaken.

Results: High levels of total IgA were observed in serum and remained unchanged from baseline, up to 28 days after challenge. Consistent with published data on infection of naïve volunteers in such a setting, levels of IgA antibody against the O antigen increased in the serum after challenge mainly in participants with clinical symptoms of disease, peaking at day 14. At the time of submission, the specific responses to the O antigen in the stool samples, in contrast, could not be correlated with clinical outcome. Nevertheless, stool anti-O antigen IgA levels in 8/14 participants increased by 2-fold or greater at day 14. A transient drop in antigen-specific IgA was observed in some participants at day 7 after challenge.

Conclusions: These are the first data on non-specific and antigen-specific IgA from stool samples during acute enteric infection. A coproantibody response specific to the pathogen was observed but no correlation could be found with clinical outcome.