



EDITORIAL

Chronic Complications After Travelers' Diarrhea

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This Editorial refers to the article by B.A. Connor and M.S. Riddle., pp. 303–312 of this issue.

Most people who develop an episode of travelers' diarrhea (TD) experience self-limiting illness with approximately 1 day of disability¹ without further medical complications. In this edition of the Journal, Connor and Riddle describe the available literature related to three well-defined complications of enteric infection including reactive arthritis (ReA), Guillain–Barré syndrome (GBS), and post-infectious irritable bowel syndrome (PI-IBS).² The review by Connor and Riddle focuses on these complications that have occurred following enteric infection of non-travelers. We do not know if these complications of enteric infection are seen with any importance in returning travelers. My comments will also relate to these post-enteric infection complications largely of non-travelers.

ReA or GBS develop from 1 to 4 weeks after enteric infection consistent with an immune disorder, while it may take months for PI-IBS to evolve. Of the three medical complications, the pathogenesis of GBS is best understood. Host antibodies directed at an infecting strain of *Campylobacter* secondarily react to central nervous system gangliosides causing the disease as an example of autoimmune molecular mimicry.³ In ReA, microbial antigens appear to reach the joint tissue and elicit an immune response in susceptible persons.⁴

PI-IBS is a distinct entity where Rome II or Rome III defined IBS develops after a bout of acute diarrhea or gastroenteritis.⁵ In this condition, a chronic low grade intestinal inflammation develops in susceptible persons after the initial enteric infection.⁶ In most studies of TD, the subjects have not been followed up sufficiently long to document this complication. Two follow-up studies have suggested that approximately 10% of patients with TD develop PI-IBS.^{7,8} The majority of patients seen

in a general population with IBS are considered to have an idiopathic form of the disease without history of antecedent enteric infection. We demonstrated that among interviewed patients attending a general gastroenterology clinic in Houston, 8% of patients with idiopathic IBS and 16% of patients with PI-IBS gave a history of international travel 6 months before onset of their chronic gastrointestinal disease⁹ suggesting the possibility that their enteric infection during travel contributed to their chronic illness.

Infection by invasive and/or inflammatory bacterial pathogens more commonly leads to later development of ReA or to PI-IBS in susceptible persons than is seen for organisms producing secretory diarrhea without mucosal inflammation such as enterotoxigenic *Escherichia coli* often seen infecting travelers with diarrhea, although many different enteropathogens appear capable of triggering the events resulting in one of the chronic complications. For GBS, the preceding enteric infection is characteristically caused by a *Campylobacter jejuni* strain. The invasive and inflammatory pathogens including *Campylobacter* are more commonly seen in TD cases occurring in Southern Asia, as studied in India or Thailand.^{10,11} It is reasonable to assume that ReA, GBS, and PI-IBS would more commonly occur in travelers to Asia experiencing TD when compared with travelers going to Latin America or Africa.

It is unlikely that all people are susceptible to one of these post-TD complications. Host genetics are involved with susceptibility to pathogen-specific TD and each of the three post-enteric-infection complications has been shown to occur more commonly in persons positive for specific and definable genes.^{12–14}

If the chronic complications of TD described herein and possibly others are found to occur with significant frequency in travel medicine, the importance of prevention of TD should be given a higher priority than is currently the case. TD prevention may be through vaccines¹⁵ or by chemoprophylaxis¹⁶ strategies.

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It is well known that treatment of TD with antibiotics can shorten the clinical course of TD, underscoring the importance of bacterial enteropathogens as causes of the disease. When therapy was begun 1 to 3 days after onset of TD in one study, later development of PI-IBS was not prevented.⁷ What is not known is whether curative treatment administered rapidly with passage of the first unformed stool passed would more importantly prevent complications. This approach may not reduce the occurrence of ReA or GBS where infection without illness may be sufficient to illicit an immune response or to deposit antigen in joint tissues. Asymptomatic infection is common in TD where contaminated foods are recurrently consumed.¹⁷ It is known that asymptomatic infection by *C jejuni* can lead to GBS.¹⁸

Researchers working in travel medicine need to routinely follow up their patients for at least 6 months after development of TD to look for occurrence of long-term complications. Systematic follow-up of travelers to their home destination is needed to determine the importance of chronic complications of TD more broadly and to characterize the pathogenesis of disease. Such study may be possible in the ISTM sponsored GeoSentinel network or in EuroTravNet.^{19,20} We need to document these conditions to see if they do complicate TD in making plans for more aggressive control and prevention strategies.

Declaration of Interests

The author states that he has no conflicts of interest to declare.

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