Long-Term Consequences of Foodborne Infections

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KEYWORDS

• Chronic bowel disorders • Autoimmune disorders • Neurologic dysfunction
• Renal failure

KEY POINTS

- Foodborne infections with *Campylobacter*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Salmonella*, *Shigella*, *Toxoplasma gondii*, and other pathogens can result in long-term sequelae to numerous organ systems.
- Prominent sequelae of foodborne infection include irritable bowel syndrome, inflammatory bowel diseases, reactive arthritis, hemolytic-uremic syndrome, chronic kidney disease, Guillain-Barré Syndrome, neurologic disorders from acquired and congenital listeriosis and toxoplasmosis, and cognitive and developmental deficits due to severe acute illness or diarrheal malnutrition.
- Evidence-based patient management and estimates of burden of disease used in public health and food policy should incorporate established and quantified long-term outcomes.
- For many chronic sequelae, disease mechanisms and the etiologic role of specific pathogens need further elucidation, as do the relative risks of sequelae following infection.
- Well-designed, large-scale, long-running prospective studies that account for the complicated interactions of host, environment, and microorganism are critical to improving our understanding of the long-term consequences of foodborne infection.

INTRODUCTION

Foodborne pathogens are a significant cause of infectious disease, resulting in an estimated 48 million illnesses, 128,000 hospitalizations, and 3000 deaths annually in

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the United States.[1,2] In addition to these acute illnesses, however, many foodborne bacteria, viruses, and parasites can result in long-term sequelae to gastrointestinal, immune, nervous, respiratory, cardiovascular, endocrine, and hepatic systems. However, because these manifestations may not arise for weeks, months, or even years after infection, they are difficult to characterize and therefore too often neglected by clinicians and public health officials alike.

Considering the long-term consequences of foodborne infections is important for patient management and setting priorities for public health. The aforementioned incidence estimates from the Centers for Disease Control and Prevention (CDC) are invaluable for the latter, but provide only a limited picture, as they include only acute illnesses and do not include any accounting of latent, chronic, or congenital sequelae. Integrated approaches to estimating the burden of foodborne disease, on the other hand, such as those that estimate annual disability-adjusted life years (DALYs), quality-adjusted life years (QALYs), or economic costs, are better able to capture the full scope of symptoms, severities, and outcomes of foodborne disease.[3–7] These studies develop disease outcome trees that resemble the decision trees used in medical decision making; they characterize the likelihoods of major outcomes based on available evidence. When long-term sequelae are included in burden of disease studies, the impacts are significant. Over half of the estimated costs in the United States associated with *Campylobacter*, for example, are due to subsequent Guillain-Barré syndrome (GBS).[5] In Dutch estimates more inclusive of sequelae, chronic morbidity is responsible for 42% of the total disease burden of 14 major foodborne pathogens.[7]

Burden-of-disease studies and clinical guidelines both rely on evidence of the etiologic role of specific agents in specific long-term sequelae. These data, drawn from epidemiologic studies and clinical practice, range from convincing to anecdotal. For many long-term conditions, the disease mechanism and the relative risk associated with specific microbial causes require further elucidation. There are several challenges to establishing causality for postinfectious chronic conditions, including, but not limited to: (1) latency between infection and sequelae; (2) complicated disease mechanisms with environmental, host genetic, and microbial genetic factors; (3) the role of coinfection and acquired host characteristics; (4) technical barriers to detecting or isolating certain pathogens; (5) the lack of systematic data collection on long-term follow-up care; and (6) the lack of necessary prospective epidemiologic studies.[8–11]

This brief overview of long-term consequences of acute foodborne illness centers on the most prominent sequelae: irritable bowel syndrome (IBS), inflammatory bowel diseases (IBDs), reactive arthritis, GBS, neurologic disorders from acquired and congenital listeriosis and toxoplasmosis, hemolytic-uremic syndrome (HUS), and attendant systemic sequelae, as well as a few others. Pathogens include *Campylobacter*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Salmonella*, *Shigella*, *Toxoplasma gondii*, and *Yersinia enterocolitica*, among others. **Table 1** presents the most prominent sequelae associated with major foodborne pathogens while **Table 2** lists sequelae for less common infections and intoxications. This review is neither comprehensive nor systematic, and reflects a body of scientific literature that often lacks consensus. The authors use best judgment, and characterize the strength of etiologic evidence where possible. References are limited and tend toward reviews, as length restrictions prevent a fuller account of relevant primary sources.

CHRONIC BOWEL AND GASTROINTESTINAL DYSFUNCTION

The symptoms of acute gastrointestinal illness are generally self-limiting, although persistent infection is common with foodborne parasites such as *Cryptosporidium*,