Risk Factors for Endovascular Infection Due to Nontyphoid Salmonellae

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(See the article by Hsu et al. on pages 829–34)

Nontyphoid salmonellae are major causes of foodborne infection worldwide. They still seriously affect human health, causing morbidity and mortality. They induce severe salmonellosis, even in modestly immunocompromised hosts, resulting in bacteremic spread, focal infection, and persistence in deep sites, including the endovascular region. Approximately 5% of individuals with gastrointestinal illness caused by nontyphoid salmonellae develop bacteremia. Children with certain underlying conditions or risk factors are at increased risk for bacteremia, which may lead to extraintestinal focal infection. These conditions and risk factors include very young age (<3 months), AIDS, presence of malignancies, receipt of immunosuppressive therapy, hemolytic anemia, and inflammatory bowel disease, among others [1–3]. In adults, nontyphoid Salmonella bacteremia is even more serious in patients with underlying disease because of both the tenacity of the organism and the multiple underlying diseases of adult patients who develop bacteremia.

A feared complication of Salmonella bacteremia in adults is the development of infectious endarteritis, especially that which involves the abdominal aorta (also known as “aortitis” or “mycotic aneurysm”), because this complication previously was almost uniformly fatal. However, a recent review of 136 evaluable cases from 1948–1999 found a 62% survival rate (mortality rate, 38%) for all affected patients who were treated with combined surgical and medical therapy [4]. In this issue of Clinical Infectious Diseases, Hsu et al. [5] report the findings from a study of 301 patients with nontyphoid salmonellosis who were seen at National Taiwan University Hospital (Taipei, Taiwan). Thirty-six people died in the hospital, including 4 patients with endovascular infection. The mortality rate among 28 patients with endovascular infection was 14.3%, which, when the severity of the condition is considered, is not higher than the rate for patients with bacteremia or other extraintestinal focal infections [5]. This low mortality rate was attained apparently with use of advanced diagnostic techniques, surgical care, and antimicrobial therapy, all of which appear to have improved the survival rate for patients with serious complications of nontyphoid Salmonella bacteremia. However, a cautious approach is still warranted, especially for older patients with multiple underlying diseases. The study by Hsu et al. [5] was a retrospective survey, and, therefore, a patient regarded as having primary extraintestinal infection might not, in fact, have had the attributed condition, because the patient might initially have had relatively mild enteritis and presented to the hospital only when he or she developed more-serious symptoms, such as bacteremia. This might be one reason that the incidence of primary bacteremia due to group B salmonellae reported in the article by Hsu et al. [5] is much higher than that reported by others [2, 6].

In their calculation of the risk factors for severe salmonellosis, such as extraintestinal infection, Hsu et al. [5] used serogroup as a variable, rather than individual serotype. Generally, in most hospitals, the etiologic agent Salmonella species is identified only to the level of serogroup, and Hsu et al. [5] were probably unable to identify the serotype further because the study was retrospective. This creates another uncertainty, because the ability of a serotype member of a serogroup to cause extraintestinal infection varies. In a recent review of literature about Salmonella aortitis, the serotypes most commonly isolated were Salmonella enterica serotypes Typhimurium, Enteritidis, and Choleraesuis, in that order [4]. In Taiwan, Chiu et
al. [2, 6] reported the order of prevalence to be S. Typhimurium, S. Choleraesuis, and S. enterica serotype Schwarzengrund; Hsu et al. [5] reported that the order is group B, group D, and then group C salmonellae. Interestingly, the reports of a relatively high incidence of S. Choleraesuis infection came mostly from Taiwan [2, 6, 7], and this distribution of serogroups was also pointed out in the report by Hsu et al. [5]. Furthermore, Hsu and colleagues concluded that Salmonella serogroup C was the only positive predictor identified for endovascular infection in adult patients with nontyphoid Salmonella bacteremia [5]. A large-scale survey from the same area [6] found that S. Choleraesuis was the most common serotype among serogroup C isolates and that, of all serotypes isolated, it had the greatest ability to cause extraintestinal infection. Therefore, the most prominent serotype among serogroup C salmonellae reported by Hsu et al. [5] was probably S. Choleraesuis; this finding is consistent with the earlier observation mentioned above [6]. Serogroup C is an imprecise classification in analysis of the properties of salmonellae. For example, S. Choleraesuis exhibits the highest level of invasiveness (measured in terms of invasion index—i.e., number of extraintestinal infections divided by total number of infections), followed by S. enterica serotype Dublin and S. Enteritidis [2, 6]. The invasion index varied greatly among the members of a serogroup—from 0 to 97 for group C, for example [2, 6]. Hsu et al. [5] are aware of this, because they discussed it in the Discussion section. S. Choleraesuis (a group C Salmonella organism) has the highest invasion index; this supports the conclusion that infection with group C Salmonella organisms is the only significant bacterial risk factor for endovascular infection.

S. Choleraesuis appears to be an uncommon serotype among human sources in Canada, the United Kingdom, and the United States [8–10]. The reason for the difference in serotype distribution between Taiwan and Western countries is of interest. In Taiwan, consecutive, hospital-based surveillance studies revealed that the mean annual number of S. Choleraesuis isolates recovered from patients in a 3500-bed medical center during 1987–2000 was 35 [11, 12]. The proportion of S. Choleraesuis isolates among all Salmonella isolates had been constant before 1995, and it decreased from a mean of 8.4% in 1995 to 2.7% in 1996–1998 [11, 12]. During 1999–2000, however, the proportion increased to a mean of 5% [11, 12]. In one study, the transient decrease during 1996–1998 was attributed to an outbreak of foot-and-mouth disease in swine, which resulted in an islandwide slaughter of pigs [12]. That study also demonstrated that most S. Choleraesuis isolates recovered from humans and swine exhibited the same or similar DNA fingerprints, indicating that human infections were derived from pigs [12]. This cross-infection was likely a result of contamination of the food or water source by this particular organism. It is also speculated that consumption of locally supplied pork, which is a staple food in Taiwan, significantly contributes to the prevalence of S. Choleraesuis infection in this region.

In addition to specific serotypes that were associated with Salmonella endovascular infection, old age was also identified as an important risk factor in the report by Hsu et al. [5] and in other, earlier studies [4, 7]. Age-related degenerative diseases, such as atherosclerosis, may be a factor that directly predisposes older patients with nontyphoid salmonellosis to endovascular infection [5]. Unfortunately, most data on risk factors are analyzed retrospectively, and, consequently, the precise risk factors remain unclear. Therefore, a prospective case-control study is urgently needed.

References