Another Perfect Storm: *Shigella*, Men Who Have Sex with Men, and HIV

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(See the article by Aragón et al. on pages 327–34)

Shigella species are a significant cause of bacterial dysentery worldwide, with ~165 million cases every year, leading to 1 million deaths annually [1]. Nearly 450,000 *Shigella* infections, causing significant morbidity, are reported each year in the United States [2]. Many of these cases occur in children or in health care institutions or are imported through travel abroad. In the mid-1970s, outbreaks of *Shigella* infection among adults in New York and San Francisco raised the possibility that *Shigella* species may be sexually transmitted, with most infections occurring in men who have sex with men (MSM) [3, 4]. Since these early observations, *Shigella* infection appears to be more frequent among MSM than among other adult populations, via direct fecal-oral transmission either through accidental inoculation of contaminated stool or through direct oral-anal contact [5–9].

The efficiency of this sexual transmission is likely fueled by several elements, both biological and behavioral in nature (figure 1). A very small inoculum of *Shigella*—as low as 10 organisms—is able to cause disease [10]. Even the accidental ingestion of minute amounts of fecal material during sexual activity could deliver a sufficient inoculum. Often transmitted through ingestion of contaminated food or water, *Shigella* species survive the chemical barriers of the stomach and thrive in the colon, leading to tissue invasion and disease [11]. Biological factors in the host likely also participate in the apparent frequency of *Shigella* infection among MSM; the immunodeficiencies related to the high prevalence of HIV infection among these men may drive transmission [8, 12]. Social adaptation by MSM in the age of HAART may affect behaviors that influence transmission of enteric pathogens, and travel-related infections may introduce *Shigella* species to networks of susceptible persons.

The study by Aragón et al. [13] is a significant contribution to our knowledge of sexually transmitted enteric infections among MSM. Their analysis of shigellosis in San Francisco through a case-control study deepens our understanding of the association between *Shigella* infection and specific sexual behaviors. The authors extend the work of Baer at al. [8], associating specific behaviors with risk for shigellosis among MSM, and strengthen the connection between HIV infection and this enteric pathogen. By analyzing cases in women and men separately, the authors highlight the likely efficient transmission of *Shigella* species in MSM. They also raise important questions about the role of HIV infection in the venereal transmission of this pathogen. The model of *Shigella* infection offered by this study represents a "perfect biological storm": a highly infectious organism imported into a behavioral setting in which continuing transmission can occur among a particularly susceptible population (figure 1).

HIV infection has several effects on *Shigella* transmission. Immunocompromised persons may have extended carriage of *Shigella* species and may have prolonged symptomatic or asymptomatic shedding at high titer. HIV infection also may have nonbiological effects on behaviors that may influence the transmission of *Shigella* infection and other sexually transmitted infections among HIV-positive MSM. Whether as a result of increased high-risk activity among HIV-positive persons or of efforts among HIV-positive men to prevent the spread of HIV infection by limiting risky sexual behaviors to partners who are already HIV positive, in the post-HAART era, *Shigella* infection, like other sexually transmitted infections, may follow specific MSM sexual networks [14]. Behaviors such as serosorting, strategic positioning, and intentional unsafe anal intercourse with others who are HIV positive may create sexual and behavioral networks of HIV-positive men that poten-

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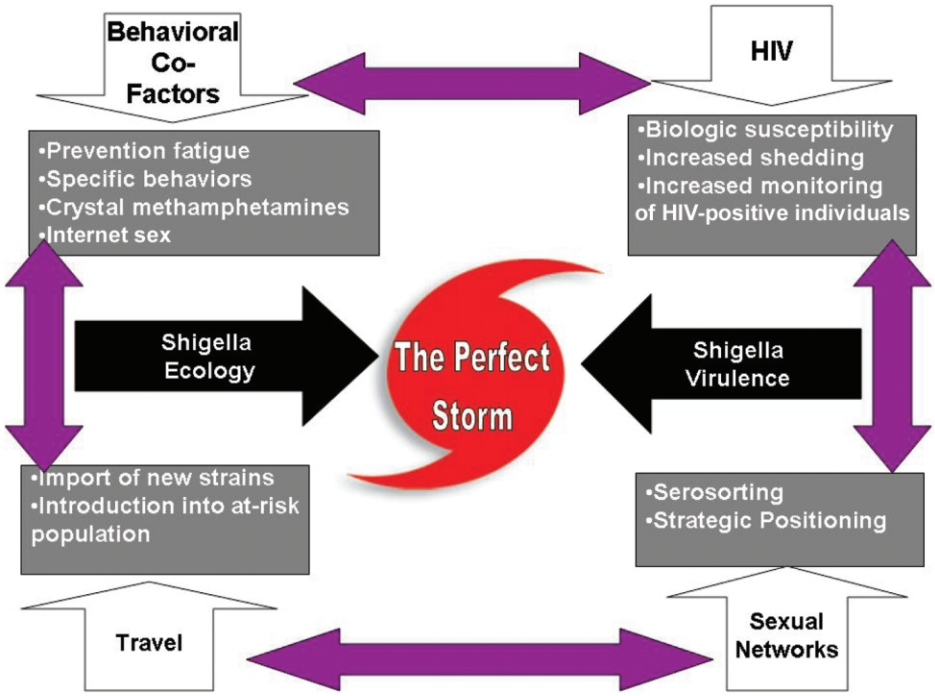

Figure 1. Factors that contribute to potentiate transmission of *Shigella* species among men who have sex with men (MSM). Because of its virulence and ecology, *Shigella* is easily transmitted in the appropriate context. Specific sexual behaviors among MSM may provide a platform, further enhanced by biological susceptibility caused by HIV-associated immunodeficiency. Changing behaviors among MSM also may create more-insular sexual networks that lead to isolated *Shigella* outbreaks within that community. Travel-related infection may serve to import infection into closed sexual or social networks to create a "perfect storm" of hyperefficient transmission of *Shigella* species.

tially enhance sexually transmitted infections among themselves but limit transmission to those who are seronegative for HIV [15].

Are HIV-positive MSM more susceptible to shigellosis, or do the specific behaviors of HIV-positive men create sexual networks that facilitate transmission to other HIV-positive men? Or are both true? Several recent studies have shown that unsafe sexual behavior has been increasing among both HIV-positive and HIV-negative MSM [16–18]. Whether this increase is influenced by optimism regarding HIV treatment, increased sex partnering through the Internet, or the impact of crystal methamphetamine use, some MSM are exhibiting higher-risk behaviors [19]. In recent years, improved sanitation and hygiene have reduced waterborne and foodborne *Shigella* species transmission and have led to a marked reduction in endemic infections in the developed world, except in certain special populations [20]. In contrast, diminished "sexual hygiene" in the form of a resurgence of high-risk behavior with multiple and concurrent partners may create endemicity for shigellosis among some groups of MSM and may generate efficient and sustained transmission networks among them [21].

An alternative possibility is that some MSM may be engaging in activities, such as serosorting or strategic positioning, that create separate sexual networks that are based on perceived HIV status. Serosorting is defined as having sex with partners of the same HIV status. Strategic positioning is changing specific sexual practices on the basis of an assumed understanding of the magnitude of the HIV infection risk that these practices incur. An example of strategic positioning is the conscious decision of an HIV-negative person to avoid receptive sex with HIV-positive partners but to still participate with them in other sexual activities that are perceived to be lower risk. The 2004 outbreak of lymphogranuloma venereum in The Netherlands, which occurred among predominantly HIV-positive MSM engaging in "leather parties," and its subsequent spread to a similar US population highlights the need for further study of the transmission of sexually transmitted infections among MSM networks to interrupt and prevent such occurrences [22].

As was the case in the 2004 lymphogranuloma venereum outbreak, travel likely plays an important role in introducing *Shigella* species to populations at risk. The predominant species of *Shigella* causing disease in MSM reported by Aragón et al. [13] was *Shigella flexneri;* however, there was an outbreak of shigellosis due to *Shigella sonnei* in San Francisco after their data collection was complete, predominantly among HIV-positive MSM [5]. This outbreak broadens our view of the transmission dynamics of *Shigella* species in that population: *S. sonnei* was likely imported via travel into a sexual network, allowing for biobehavioral amplification

into an outbreak. The replacement of *S. flexneri* by *S. sonnei* may reflect some degree of herd immunity in the core population. In association with import through travel, factors including immunodeficiency, seropositive sexual networks, and *Shigella* virulence likely synergize to create conditions that facilitate the transmission of *Shigella* species to outbreak levels among HIV-positive MSM (figure 1).

This study raises several questions that merit further investigation. Do CD4 cell counts and other measures of immune status affect why HIV-positive MSM are more likely to develop shigellosis? Are there other behavioral or biological correlates of susceptibility to *Shigella* species in this population? Does HIV infection status affect the frequency of direct or indirect anal contact by MSM? Which steps are needed to interrupt transmission of enteric pathogens through sexual networks? How do serosorting, strategic positioning, and other behavioral cofactors influence transmission of *Shigella* species? Are HIV-positive women at increased risk for shigellosis?

Aragón et al. [13] have demonstrated a convincing association between *Shigella* species, specific sexual activities between men, and HIV status. The elements that combine to create this "perfect storm" of disease transmission already allow public health recommendations to permit their interdiction.

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