Connecting the Dots: Could Microbial Translocation Explain Commonly Reported Symptoms in HIV Disease?

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Microbial translocation within the context of HIV disease has been described as one of the contributing causes of inflammation and disease progression in HIV infection. HIV-associated symptoms have been related to inflammatory markers and sCD14, a surrogate marker for microbial translocation, suggesting a plausible link between microbial translocation and symptom burden in HIV disease. Similar pathophysiological responses and symptoms have been reported in inflammatory bowel disease. We provide a comprehensive review of microbial translocation, HIV-associated symptoms, and symptoms connected with inflammation. We identify studies showing a relationship among inflammatory markers, sCD14, and symptoms reported in HIV disease. A conceptual framework and rationale to investigate the link between microbial translocation and symptoms is presented. The impact of inflammation on symptoms supports recommendations to reduce inflammation as part of HIV symptom management. Research in reducing microbial translocation-induced inflammation is limited, but needed, to further promote positive health outcomes among HIV-infected patients.

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Insights into the pathogenesis of HIV infection have implicated microbial translocation as one of the key drivers of HIV disease progression and inflammation

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(Brenchley & Douek, 2008; Brenchley et al., 2006; Marchetti et al., 2011; Sandler et al., 2011). Microbial translocation is the movement of bacteria and/or microbial products from the gut to the bloodstream. Commonly reported gastrointestinal (GI) and systemic symptoms may have a relationship with chronic inflammation induced by circulating microbial products from the GI tract in patients with HIV disease. Even with effective combination antiretroviral therapy (cART) and viral suppression, inflammation from chronic immune activation increases the rates of morbidity and mortality among people living with HIV disease (PLWH; Brenchley et al., 2006; Deeks, 2011; Kamat, Misra, et al., 2012; Marchetti et al., 2011). It is critical for nurses to have a working understanding of the concepts of microbial translocation, inflammation, and symptom management in the clinical management of HIV disease.

Background and Significance

Chronic inflammation has been identified as a key predictor in the development of comorbidities and mortality in HIV disease. One source of inflammation – the inflammation of the GI epithelial barrier – ultimately leads to dysfunction of the protective lining of the gut. Consequently, microbes naturally residing in the gut are able to pass through the gut-associated lymph tissue (GALT) into the blood circulation (Estes et al., 2010; see Table 1 for definitions). The immune system responds to circulating microbes with systemic and often chronic inflammation (Brenchley et al., 2006).

Inflammation of the GI epithelial barrier in HIV disease resembles inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). Inflammation of the GI epithelial barrier leads to symptoms including diarrhea, bloating, and abdominal pain (Berkes, Viswanathan, Savkovic, & Hecht, 2003; Epple & Zeitz, 2012). In IBD/IBS, inflammation leads to the translocation of microbes naturally residing in the gut into the bloodstream, as seen in HIV disease where microbial products residing in the gut translocate through the GALT into the bloodstream (Brenchley et al., 2006; Epple & Zeitz, 2012).

Systemic inflammation experienced chronically has been associated with systemic symptoms and conditions. Symptoms are often adverse experiences perceived from underlying changes in the biopsychosocial function of an individual. Signs and symptoms provide key assessment information to support the formulation of diagnostic pathways for clinicians. Symptoms are usually measured by self-report as opposed to a sign, which is an abnormality that can be detected by the individual and by others observing the individual (Dodd et al., 2001). PLWH often experience and report symptoms to their providers. However, the subjectivity of symptoms can limit objective assessment by another individual, creating huge challenges for clinicians and scientific investigators, as symptoms may not be objectively measured by another human being unless people report what they are experiencing.

Symptoms are often attributed to side effects of treatment with cART (Johnson, Stallworth, & Neilands, 2003). Patients initiating antiretroviral therapy in the early era of the HIV epidemic were at risk for serious adverse events and major side effects, but current cART regimens are simpler, better tolerated, more effective, and offer lower side-effect profiles than earlier regimens used in the treatment of HIV disease (Katlama et al., 2009; Lennox et al., 2009; Madruga et al., 2007). And yet, many symptoms persist in some individuals. In addition, the symptom burden experienced by PLWH has been associated with poor medication adherence, such as when people want to avoid symptoms, forget to take scheduled doses, and/or sleep through medications due to fatigue (Gay et al., 2011). Symptom burden is the summation of disease expression and/or the product of the treatment of that disease, usually referred to as the side effects of treatment (Cleeland & Reyes-Gibby, 2002).

Our purpose was to review how inflammation from HIV disease may lead to symptoms experienced by PLWH in the context of microbial translocation, as well as how this event may lead to treatment failure. We describe the process and consequences of microbial translocation and inflammation, and how this inflammatory process may be related to symptoms experienced (Figure 1). Furthermore, we address the gaps in knowledge and challenges in demonstrating a valid hypothesis linking microbial translocation and symptoms.