
Managing Fever and Febrile Symptoms in HIV: Evidence-Based Approaches

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Fever remains a common symptom for persons living with HIV (PLWH) despite improving overall health and survival rates. Elevated body temperatures are among the classic symptoms of primary HIV infection and are later harbingers of opportunistic infections. Therapeutic agents, including antiretrovirals, antifungals, interleukins, interferon, and blood products, can produce fever. While research shows that fever holds immunological benefits, and outdated practices to cool febrile patients create distress and energy expenditure from shivering, “fever phobia” persists. This article discusses the evolution of understanding about fever and HIV infection, its influence on caregivers and PLWH, and the existing evidence surrounding (a) physiological threats and benefits of the febrile response for PLWH, (b) goals underpinning assessment and management of fever and related febrile symptoms, and (c) development and testing of fever-management interventions. This evidence is summarized with rationale for the need to educate both public and professionals about the complexities of fever.

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Fever, or pyrexia, is defined as an abnormally high, but neurologically regulated, body temperature caused by host responses to either an endogenous or exogenous pyrogen (fever-producing substance; Kluger, Kozak, Leon, Soszynski, & Conn, 1995). Although temperature elevation is the most recognizable febrile sign, systemic molecular and immunolog-

ical effects are responsible for the host benefits as well as the noxious symptoms of fever (Cunha, 2012).

The Epidemiology of Fever in HIV

Fever remains one of the most common symptoms experienced by persons living with HIV infection (PLWH) despite overall health improvements and survival rates. An elevated temperature occurs early as one of the classic symptoms of primary HIV infection, or acute retroviral syndrome, in 40% to 70% of PLWH (Hot, Schmulewitz, Viard, & Lortholary, 2007). Longer-lasting fevers, without a clear etiology, are more characteristic of later stages of the disease when CD4+ T lymphocytes are extremely low. Today's antiretroviral therapy (ART) has reduced the frequency of febrile infections in seropositive patients, but the number and variety of infectious and noninfectious causes of fevers have actually increased (Hot et al., 2007). In fact, antiretroviral agents and other drugs used to treat PLWH have added to the agents capable of causing fever (Fellay et al., 2001; Silverberg et al., 2004).

Advancement of Fever Science and Treatment

Unfortunately, the translation of evidence on fever from the research bench to the clinical bedside has

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been slow, particularly as it is related to the dynamics of febrile temperature elevation and its systemic role. Even slower to evolve are applications of existing evidence for fever management into clinical practice (Thompson, Kirkness, & Mitchell, 2007), and some practices that are clearly contrary to evolving science continue. One gap in scientific translation is the lack of understanding that fever is a systemic host response and its effects are more than an elevation in body temperature. Yet many lay and professional caregivers are only familiar with the thermal responses of fever, febrile chills, and sweating (Pursell, 2009; Rupe, Ahlers-Schmidt, & Wittler, 2010). “Fever fear” beliefs consider eradication of higher temperatures as an approach to fighting disease while failing to recognize current scientific findings that document antibacterial and antiviral effects of higher febrile temperatures (Murapa, Gandhapudi, Skaggs, Sarge, & Woodward, 2007). These beliefs hold negative outcomes for the patient if caregiving focuses on cooling interventions that promote distressful warming responses such as shivering. The oxygen expenditure from shivering is poorly tolerated by vulnerable, cachectic, or weak patients (Holtzclaw, 1990c). Acute-care clinicians appear to be keenly aware that higher temperatures raise energy expenditure and caloric requirements 10% for each degree of Celsius increase (Sund-Levander & Wahren, 2000). Yet few seem to be aware of the more drastic metabolic toll that vigorous shivering causes by increasing metabolic expenditure 100% to 300%, despite well validated research dating back to the 1960s (Hemingway, 1963).

Current scientific evidence shows that elevated body temperature provides optimal conditions to promote immune factors (Jiang et al., 2000; Murapa et al., 2007), but it has taken generations of research to find out why. Scientific discoveries of the past two decades have demonstrated the proinflammatory molecular and systemic benefits of fever, but research evidence on interventions to clinically manage fever symptoms has been sparse. Furthermore, without replication or further testing, the successes of non-pharmacological fever interventions published more than a decade ago are still not part of the mainstream of current practice (Holtzclaw, 1990a; Holtzclaw, 1990b). Clinical research has been aimed primarily at antipyresis or treatment of underlying infections.

Even less research has examined fever management in the context of HIV disease. This article discusses the evolution of understanding about fever related to HIV infection and its influence on caregivers and PLWH and presents the existing evidence surrounding (a) physiological threats and benefits of the febrile response for PLWH, (b) goals underpinning assessment and management of fever and related febrile symptoms, and (c) development and testing of fever management interventions. This evidence is summarized with rationale for the need to educate both public and professionals about the complexities of fever.

The Search Strategy

A systematic search was conducted using the following databases up to March 2012: Medline, CINAHL, and the Cochrane Database of Systematic Reviews. The first set of search terms included MeSH terms *fever* and *symptoms* in various combinations with *febrile symptoms*, *symptom management*, and *symptom treatment*. Combinations of *fever and AIDS* and *fever and HIV* were searched in each database. Articles were further eliminated by relevance (Figure 1). Reference lists from selected research reports and review articles provided additional sources for the search. The search revealed that current research evidence in febrile symptom management beyond antipyretic use is sparse. Older studies are cited in this review as research evidence. These classic studies are also frequently cited in current literature because more recent research on relevant fever management topics is not available. This phenomenon can be challenging to clinicians who are urged by their training to seek out and cite only current literature.

The Evolving Face of Fever for PLWH

Early in the HIV epidemic, fever was primarily seen as an initial response to the virus itself, along with malaise, night sweats, weight loss, and diarrhea (Tindall, Carr, & Cooper, 1995). As an individual's disease progressed, fever was associated with a variety of opportunistic infections (OIs). Infections and symptom clusters, or complexes that included fever, were often predictive of death early in the

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