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Editorial

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EDITORIAL

Are 'asymptomatic' Chronic Infections Truly asymptomatic?

Last summer, while attending the Gorgas Expert Course in Tropical Medicine in Lima, Peru, I met a young man with extensive scaly, malodorous plaques on his scalp and behind his ears. I learned that the underlying condition leading to his infectious dermatitis was the same as that for an elderly gentleman we met earlier who shed blizzards of flakes from his skin due to crusted scabies. It was also the same underlying condition that led to an HIV-infected woman with a CD4 count of 700 cells/mm^3, a count well in the normal range, to develop *Pneumocystis carinii jiroveci* pneumonia, an opportunistic infection usually only seen in AIDS patients. All three of these patients were infected with the human T-lymphotrophic virus type 1 (HTLV-1). The classic teaching on HTLV-1 has been that an unfortunate ∼5% of HTLV-1-infected individuals develop either adult T-cell leukemia/lymphoma or HTLV-associated myelopathy during their lifetime, but that the vast majority of HTLV-1-infected individuals never develop clinical disease [1]. However, recent studies suggest that this might not be true. HTLV-1 infection has now been linked to infectious dermatitis [1], uveitis, pneumonitis, polymyositis, arthritis, Sjogren's syndrome, strongyloidiasis, crusted scabies [2], paracoccidiomycosis [3], and (in HIV-coinfected individuals) artificially increased but dysfunctional CD4 counts [4]. This led me to wonder: are 'asymptomatic' chronic infections ever truly asymptomatic?

Cytomegalovirus (CMV) is another cause of chronic infection that might be more detrimental than previously thought. After acute CMV infection, which can cause congenital CMV syndrome in fetuses and an infectious mononucleosis syndrome in children and adults, CMV is not cleared but remains in a latent state [5]. Although latent CMV infection can cause a number of severe syndromes due to reactivation in immunocompromised individuals, it has long been thought to cause no disease in healthy children and adults. However, a recent population-based study found that latent CMV infection is associated with a 16% increase in all-cause mortality, with most of the increased deaths attributable to cardiovascular disease and cancer [6]. It has also been shown that latent CMV infection creates a chronic inflammatory state that can lead to accelerated immune aging, or immunosenescence [7]. This CMV-associated immunosenescence may result in increased susceptibility to infections and possibly decreased protection from vaccines [8].

Clinical manifestations from 'asymptomatic' chronic infections are not limited to viruses. Acute infection from the protozoan *Toxoplasma gondii* can lead to congenital toxoplasmosis in fetuses, and chorioretinitis in a small fraction of infected children and adults [9]. After primary infection, *Toxoplasma* causes a chronic latent infection that can persist for life. Although latent toxoplasmosis can cause severe disease in immunocompromised individuals through reactivation, it is generally believed to be asymptomatic in healthy individuals. However, recent studies have suggested an association between latent toxoplasmosis and neuropsychiatric disorders in

otherwise healthy individuals, including a 3-fold higher risk of schizophrenia and a 2-fold higher risk of mood disorders [10].

These clinical complications from apparently asymptomatic infections make one wonder if a state of sterility should be aimed for, such that any infection, regardless of whether clinical symptoms are apparent, should be treated. However, we know from experience that this approach is also fraught with danger. Aside from the numerous side effects from the antimicrobial agents themselves, antibiotic use is the primary risk factor for *Clostridium difficile* colitis, as well as a risk factor for other serious infections like candidemia. Furthermore, antibiotic use (and presumably also antiviral, antiparasitic and antifungal use) disrupts the microbiome. Recent studies have linked antibiotic-associated changes in the microbiome to development of obesity and noninfectious inflammatory diseases [11]. Even *Helicobacter pylori* eradication, which has long been promoted to decrease the risk of gastric cancer, may no longer be clear cut in that recent data suggests that *H. pylori* infection may be protective against stroke [12].

All in all I think we have to accept that our bodies are not wholly our own, but are in fact hosts to billions of organisms that likely have both positive and negative effects on our health. And just like in any community, from small family units to the global community, striving for balance may be the best strategy.

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