Redefining Schistosomiasis haematobium in light of its impact on HIV transmission: an argument for reinvigorated global commitment to Schistosomiasis control.

Melissa Janssen
Op-Ed

The number of neglected tropical diseases (NTDs) that are being newly recognized as not simply diseases in their own right, but as important cofactors and exacerbaters of more highly-politicized and well-funded diseases is growing.[1] A prime example of this is *Schistosomiasis haematobium* (SH) infection – an NTD caused by freshwater-residing parasites that has recently been suggested to be more intricately tied to HIV/AIDs acquisition and transmission than researchers had previously realized.

This paper argues that SH should be globally reframed as not just an NTD, but the most important cofactor of HIV/AIDS in sub-Saharan Africa (SSA); elimination should not be considered an unattainable ideal, but a tremendously effective method of curtailing the HIV/AIDS epidemic in co-endemic regions. This redefinition could see SH control programming integrated into the widely-politicized and well-funded HIV-programming, allowing this NTD to finally receive the attention it requires. Consequently, the world could witness not only the elimination of the second deadliest parasitic infection, but an impressive assault on the HIV/AIDS epidemic that for four decades has devastated the globe.

Schistosomiasis control and elimination is believed to suffer from the single largest gap in funding, receiving "almost nonexistent global coverage".[2] This is despite the fact that over 230 million individuals succumb to infection each year, 85% of which live in rural villages in SSA, and an effective drug treatment called Praziquantel exists that costs less than 50 US cents per person to produce and distribute.[3, 4, 5]

The problem is that SH is a disabler, not a killer; it causes inflammation to the urogenital regions and significant chronic disabilities that afflict and impair an individual for most of their lifetime, but the infection itself is not fatal.[6] More deadly diseases like HIV/AIDs have continually dominated the funding and research agendas of most countries and institutions.

Indeed, all five species of schistosomiasis combined received a mere 1.6% of the funding allocated towards HIV/AIDs research and development in 2008.[7] More, the world was able to make available $19.2 billion for HIV/AIDS in 2014, and in 2012, approximately 60% of all eligible individuals in SSA gained access to anti-retroviral therapy (ART).[8, 9] This is in direct comparison to the 14% who had access to Praziquantel that same year.[10] Globally in the last 5 years, the amount of people gaining access to lifesaving ART has tripled; conversely, the number of individuals gaining access to lifesaving Praziquantel has risen by approximately 2 percent.[10, 11]

However, there is an ironic twist in this tale of neglect. There is a multitude of recent evidence suggesting, and in some cases confirming, a pathophysiological association between SH and HIV/AIDS. If this association can be accepted by the scientific community at large, the elimination of schistosomiasis could be considered a legitimate strategy for HIV prevention.

Not only is there a striking epidemiological overlap between SH and HIV/AIDs, but several demographic trends reinforce this possible relationship. The significant majority of HIV/AIDs sufferers across the globe are men.[11] However, in SSA, where the majority of female SH cases are found, nearly 60% of HIV/AIDs victims are women; here, there are 1.3 - 6.4 HIV-positive women for every man, depending on the region.[12] More, among women in SSA, the prevalence of HIV is greater among those in rural communities and peaks at a younger age compared to urban regions.[13] This suggests there may be risk factors in rural villages – such as the presence of SH in bodies of freshwater where women typically perform domiciliary tasks – that differ from risk factors in urban regions and thus influence HIV prevalence.

Studies in both Zimbabwe and Tanzania have sought to quantitatively assess whether SH is an important cofactor in HIV/AIDS acquisition and

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Melissa Janssen
Op-Ed, *cont'd*

transmission.[13, 14] These studies not only demonstrate a strong correlation between the presence of SH and HIV clinical indicators, but demonstrate that women suffering from SH were 2 to 4 times more likely to be co-infected with HIV, lending groundbreaking plausibility to this association.

Another group of researchers conducted an innovative alternative to these somewhat limited cross-sectional studies. Georeferenced information contained in the AIDS Indicator Survey was linked with the Global NTD open-source database in order to construct a schistosomiasis exposure covariate in Mozambique.[15] In "logistic regression analyses predicting HIV-positive status", this group showed that "exposure increases the odds of HIV-positive status by three times, controlling for demographic and sexual risk factors".[15]

From a pathophysiological perspective, this association is plausible. The hypothesis is that the mechanical breach of the genital mucosa caused by active SH infection, as well as the egg-induced neovascularization surrounding lesions, creates direct points of contact between HIV and the receptive cells of the woman, rendering SH-infected females more prone to contracting or transmitting HIV during intercourse.[16, 17, 18, 19] As well, the SH-induced inflammation recruits significant numbers of CD4+ cells to the damaged area, all of which possess the primary cellular receptor for HIV.[17] The lymphocytes recruited to the area are characteristically Th2 T-cells as opposed to Th1.[16] This Th2 response induces accelerated replication of HIV as a result of the stimulatory effect of several Th2-associated cytokines, namely IL-6 and TNF-alpha.[18] More, it upregulates the HIV co-receptors CCR5 and CXCR4 on the surface of the local lymphocytes and monocytes, and is associated with a reciprocal downregulation of the Th1 response.[14, 20] This results in diminished cytotoxic T-cell function and thus, diminished ability to control HIV infection. [16]

In males, SH infection and inflammation is accompanied by lower volumes of semen and significantly higher volumes of inflammatory cytokines in the seminal fluid.[16] These increased cytokines and inflammatory markers "recruit more HIV-infected cells to the semen, upregulate viral replication, and increase the concentration of HIV in the seminal fluid".[16] Therefore, a female sexual partner automatically has an increased risk of contracting HIV, with or without concurrent schistosomiasis infection. Disturbingly, however, a woman with an established SH infection has a doubly-amplified risk of contracting HIV: "her SH-infected partner's semen may contain disproportionately high concentrations of HIV RNA, and her own SH infection may increase the ease with which HIV can establish infection following exposure".[16]

The WHO has published their Priority Interventions 2010 report which delineates for decision making bodies the HIV/AIDS health interventions the WHO regards as paramount.[21] Notably but not surprisingly, the elimination of SH and other relevant NTDs are not mentioned. They have, however, listed a set of criteria they believe any intervention must possess for them to be deemed priorities according to WHO standards. The interventions must be: (a) feasible, (b) locally appropriate, (c) equitable, (d) based on evidence and good practice, (e) take into consideration cost effectiveness and sustainability, (f) avoid possible negative effects on other health outcomes, and (g) synergistic with other health interventions. Our group has found through extensive research that the four pillars of schistosomiasis control and elimination programming – namely, mass drug administration, snail control, WASH programming, and other educational campaigns – adequately satisfy all of these criteria. Thus, there are legitimate grounds upon which one can propose that the historically neglected schistosomiasis programming can and should be incorporated into HIV prevention mechanisms.

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Melissa Janssen
Op-Ed, *cont'd*

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