Does S. mansoni treatment affect HIV susceptibility?

Young women and children carrying out their daily activities in Lake Victoria, an area endemic for Schistosoma mansoni. Bugonga, Wakiso District, Uganda (Photo by S. Yegorov).

Schistosomiasis is a water-borne disease caused by helminths known as schistosomes, in which adult worms deposit eggs in the blood vessels around internal organs such as the intestine or bladder. Schistomiasis is endemic to many tropical regions, including fishing communities in East Africa where prevalence often exceeds 60% in the Lake Victoria region and overlaps with a high prevalence of HIV. There is evidence that schistosomiasis could enhance HIV acquisition, and this is not only pertinent to people with a genitourinary form of

schistosomiasis (caused by *Schistosoma haematobium*), but also to those people who carry “intestinal” schistosomiasis caused by *S. mansoni*. Epidemiological investigations in the Lake Victoria region (Tanzania) found an association between *S. mansoni* and HIV infection, an effect most pronounced in adult women. Furthermore, in animal model studies *S. mansoni* infection increased susceptibility to simian HIV after rectal- but not intravenous- challenge. This suggests that *S. mansoni* might elevate HIV susceptibility by changing mucosal gut immunology. While the exact biological mechanisms of this association remain incompletely understood, a recent study sheds light on the effect of *S. mansoni* treatment on HIV susceptibility in women.

In their study, Yegorov et al., employed *ex vivo* HIV entry assays in combination with flow cytometry, cytokine measurements and transcriptome analysis to gain insight on how standard praziquantel schistosomiasis therapy affects systemic and genital immunology of Ugandan women. The authors found that *S. mansoni* treatment induced a reduction of *ex vivo* HIV entry into cervical and blood CD4+ T cells that lasted for up to two months. Interestingly, the researchers also observed transient systemic and mucosal immune activation immediately after *S.mansoni* treatment, attributing this to an induction of acute pro-inflammatory and antiviral pathways. They indeed found that genital IFN-α2a levels were elevated in the participants post-treatment, while RNA-sequencing analysis of blood mononuclear cells indicated IFN-I pathway up-regulation and partial reversal of helminth-dysregulated interferon signalling associated with *S.mansoni* therapy.

These results together with the evidence from earlier studies suggest that *S. mansoni* treatment could help reduce HIV transmission by having a direct beneficial impact on antiviral immunity. Larger clinical trials will be necessary to validate these findings and the public health importance of mass *S.mansoni* treatment for HIV acquisition. Fortunately,

praziquantel, the current standard for schistosomiasis treatment, is very safe and affordable, being an ideal choice for preventive deworming programs that are already underway in some regions with high disease burden.

Visual Summary of this research is available as part of the Immunopaedia-Keystone initiative

Journal Article: Yegorov S. *et al* (2019) *Schistosoma mansoni* treatment reduces HIV entry into cervical CD4+ T cells and induces IFN-I pathways. Nat Commun.

Other References :

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- Downs, J. A. et al. (2017) Effects of schistosomiasis on susceptibility to HIV-1 infection and HIV-1 viral load at HIV-1 seroconversion: A nested case-control study. PLoS Negl Trop Dis.
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