

Establishing a Female-only Controlled Human *Schistosoma mansoni* Infection Model: a safety and dose finding study

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A controlled human infection model with schistosomiasis (CHI-S) has the potential to speed up vaccine development and can provide useful insights into immune responses following exposure to schistosomes. Recently, a CHI-S model was successfully established using only male *Schistosoma mansoni* (*Sm*) cercariae in Dutch *Schistosoma*-naïve individuals. In this current study, we aimed to establish a single-sex, female-only CHI-S model to identify which dose of female *Sm* cercariae is safe and leads to patent infection. To this end, we enrolled 13 healthy, *Schistosoma*-naïve volunteers who were challenged with 10 (n=3) or 20 (n=10) female cercariae. Subsequently, participants were followed up for 20 weeks, receiving treatment with praziquantel twice at 8 and 12 weeks after exposure. Throughout, safety data and samples were collected. We used serum circulating anodic antigen (CAA) levels to determine infection status (≥ 1.0 pg/mL). In addition, we monitored eosinophil levels and *Schistosoma* serology. So far, 6 participants have completed the 20 week follow-up, while the remaining 7 participants are scheduled to complete week 8 mid-June. Similar to the male CHI-S, we observed a rash at the site of infection in nearly all participants. Starting three weeks after exposure, participants reported systemic symptoms probably related to acute schistosomiasis. None of the participants exposed to 10 cercariae showed CAA levels above 1.0 pg/ml, while in the 20 cercariae dose group 2 out of 3 did. Based on these preliminary data, the safety profile of female cercariae seems similar to that of male cercariae. This female CHI-S model together with the previous male CHI-S model provide unique opportunities to dissect sex-specific immune responses to *Schistosoma mansoni* that can further vaccine development.