Development of a Rectal Sexually Transmitted Infection (STI) Model in Rhesus Macaques using *Chlamydia trachomatis* serovars E and Lymphogranuloma Venereum, type 2

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**Background**

New animal models are needed to augment efficacy testing of biomedical HIV preventions and better understand susceptibility factors for transmission relevant to men who have sex with men (MSM). A rectal STI coinfection macaque model could provide such conditions of enhanced susceptibility.

**Materials and Methods**

Rhesus macaques (n=9) were rectally inoculated with one of three *Chlamydia trachomatis* infection strategies: Lymphogranuloma venereum, type 2 (LGV-2) alone (n=3); *C. trachomatis* serovar E (CT-E), followed by LGV-2 (n=3); and CT-E, CT-E treatment and clearance, then LGV-2 (n=3). All three groups included a baseline period and individual infection, treatment and test-of-cure, and follow-up periods spanning three weeks. STIs were monitored by Aptima (Hologic) testing. Weekly blood and rectal sponge secretion collections were used for systemic and mucosal cytokine analyses, respectively, using Luminex technology. Weekly rectal lavage supernatants were assayed for epithelial sloughing by microscopy. Weekly fecal samples and rectal lavage supernatants were assayed for occult blood with the Hemoccult II SENSA kit (Beckman Coulter). Rectal sponge
and lavage supernatants were visually inspected for overt blood presence. Periodic rectal biopsies were evaluated by histopathology for tissue integrity and cell infiltrate.

Results

CT-E and/or LGV-2 infections were successfully established in each animal, with varying degrees of persistence over respective infection periods. No evidence of systemic inflammation was observed through plasma cytokine analysis. Evidence of mucosal inflammation was seen with the upregulation of IL-1ra post-infection in all three experimental groups (p>0.05, Wilcoxon rank sum). Epithelial sloughing was observed in all three groups, but to the greatest degree in animals infected consecutively with CT-E and LGV-2 (sloughing at 61% of post-infection time points, persisting into treatment and follow-up phases). Overt and occult blood was detected in all groups post-infection, but also to a small degree at baseline sampling. Rectal blood detection was more frequent in groups infected with CT-E and LGV-2, compared to LGV-only. Rectal biopsy histopathologic analyses revealed mild edema and lymphoplasmacytic infiltrates in two of three macaques infected consecutively with CT-E and LGV-2.

Conclusions

These pilot data and observations demonstrate the successful infection of rhesus macaques with CT-E and LGV-2 by different experimental approaches and describe the use of various measures by which to assess inflammation and pathology in the rectal mucosa. The different infection strategies yielded varying inflammatory and pathologic outcomes, providing a set of well-described pilot models for future studies of enhanced susceptibility to rectal SIV or SHIV infection. Furthermore, the use of a model employing multiple rectal infections, as well as those commonly found in MSM, supports the model’s future relevance for this demographic and the domestic HIV epidemic.

Disclaimer: The findings and conclusions in this abstract are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.