2020

Effect of Physical Maturation and Sexual Debut on HIV Susceptibility in Adolescent Males in Rakai, Uganda

Zhongtian (Eric) Shao
University of Western Ontario, zshao52@uwo.ca

Godfrey Kigozi
Rakai Health Sciences Program

Ronald M. Galiwango
Rakai Health Sciences Program

Cindy Liu
George Washington University

Rupert Kaul
University of Toronto

See next page for additional authors

Authors

Zhongtian (Eric) Shao, Godfrey Kigozi, Ronald M. Galiwango, Cindy Liu, Rupert Kaul, Aaron AR Tobian, and Jessica Prodger

Effect of physical maturation and sexual debut on HIV susceptibility in adolescent males in Rakai, Uganda

Zhongtian Shao[1], Godfrey Kigozi[2], Ronald M Galiwango[2], Cindy Liu[3], Rupert Kaul[4], Aaron AR Tobian[5], Jessica L Prodger[1]
[1]Department of Microbiology and Immunology, The University of Western Ontario
[2]Rakai Health Sciences Program
[3]Department of Environmental and Occupational Health, George Washington University
[4]Department of Medicine, University of Toronto
[5]Department of Pathology, Johns Hopkins University School of Medicine

Background: Global HIV-1 incidence has fallen significantly over the past decade, but HIV-1 incidence among adolescents has remained unchanged and AIDS-related deaths among adolescents have increased. Adolescents account for ~30-40% of global HIV-1 incidence with >85% of new HIV-1 infections in adolescents taking place in Sub-Saharan Africa. While the sociodemographic and behavioral factors associated with HIV-1 risk among adolescents have been well characterized, the role of the adolescent mucosa in HIV-1 acquisition remains unclear. HIV first infects immune cells in the mucosa, and mucosal inflammation is a well-characterized HIV risk factor. More recently, high abundances of certain species of anaerobic bacteria on the penis have also been identified as increasing HIV risk, and there is evidence that these bacteria may be shared between sexual partners. In this study, we aim to determine the impact of sexual debut and physical maturation on the penile microbiome, penile immunological milieu, and HIV-1 susceptibility in adolescent boys.

Hypothesis: We expect that anaerobes associated with HIV susceptibility in men will be absent from the penis prior to sexual debut, and that their introduction to the penis will be associated with increased local inflammation including the recruitment of HIV target cells. We further hypothesize that the introduction of these anaerobes and the associated inflammation will result in a period of increased HIV susceptibility in adolescent boys, with may explain the higher HIV rates in this population.

Methods: We monitored the physical maturation and sexual debut of 200 uncircumcised, sexually naive, initially HIV-1 negative boys (age 15-19) in Rakai, Uganda over 3 years. Study visits performed quarterly (every 3 months) collected data on sexual activity and physical maturation, as well as collecting blood and penile swab samples. Foreskin tissue from participants who underwent circumcision during the study period were also preserved. To evaluate whether the penile microbiome changes with physical maturation and sexual debut, we will extract and sequence bacterial DNA in penile swab samples to quantify bacteria associated with HIV-1 risk. Swab samples will also be screened for the presence of pro-inflammatory molecules previously associated with HIV risk. To evaluate the cellular and tissue level impact of sexual debut and physical maturation on HIV-1 susceptibility we will (i) quantify cells susceptible to HIV-1 and markers of epithelial barrier to HIV-1 using fluorescent microscopy, and (ii) assess the *in vitro* susceptibility of foreskin tissues to HIV-1.

Progress: Enrolment was completed in September 2017 and the 3-year follow-up will be completed in December 2020. Median monthly follow-up has been 84.3%, excluding 3 visits affected by COVID19 closures. To date, foreskin samples have been obtained from 53/200 boys, and 127 boys (63.5%) have reported initiating sexual activity while under study observation.

Impact: The HIV-1 pandemic in adolescents is growing and current prevention strategies used to control its spread remain inefficient. Our study will address a critical knowledge gap on the pathophysiology of HIV-1 risk in adolescent boys and will inform novel strategies to protect adolescents from HIV-1 acquisition.