

## Human Herpesvirus 8 Infection in Sub-Saharan Africa

**Principal Investigators:** Jeffrey Martin and Dennis Osmond, **Co-Investigators:** Nancy Padian, Lisa Butler, Alison Graves, Christian Brander, David Scadden, Anisa Mosam, Halima Dawood, and Caroline Shiboski

**Project Description :** The AIDS epidemic has dramatically altered both the epidemiology and clinical manifestations of Kaposi's sarcoma in sub-Saharan Africa. Where cancer registries are available, Kaposi's sarcoma is now the most common adult cancer, representing up to 40% of all adult malignancies, affecting women as often as men. The clinical manifestations of Kaposi's sarcoma have also changed, with the most common presentation being more aggressive forms such as those with pulmonary or gastrointestinal involvement. Consistent with its etiologic role, the prevalence of HHV-8 infection in sub-Saharan Africa is among the highest in the world with an estimated 30 to 60% of the overall population infected. Thus, we now understand how the catastrophic intersection between endemic HHV-8 infection and the epidemic of HIV infection in sub-Saharan Africa has resulted in an enormous increase in Kaposi's sarcoma incidence there.

The long-term objective of our work in Africa is to determine how HHV-8 is transmitted to children, the age group where the majority of infections are known to occur. This would enable the development of specific interventions to prevent HHV-8 transmission and/or identify those at highest risk who would be suitable for the evaluation of potential vaccine candidates. We have recently begun two studies in this region. The first is a study of 600 women of reproductive age in Harare, Zimbabwe, in collaboration with Drs. Nancy Padian and Caroline Shiboski. This population group was chosen because one of the initial hypotheses regarding HHV-8 transmission in this region suggests that mother-to-child spread is most important. The objectives of this work are to determine the prevalence and determinants of HHV-8 seropositivity among young women and the occurrence of and risk factors for HHV-8 shedding in various body fluids, such as saliva and vaginal fluids. Saliva, in particular, is being focused on because preliminary evidence suggests it is the body fluid that most commonly harbors HHV-8. The magnitude of HHV-8 shedding in saliva will be compared to HHV-8-infected persons from the US to evaluate the hypothesis that HHV-8 infection is more common in sub-Saharan Africa because of greater infectiousness (i.e., greater magnitude of viral shedding) among infected persons.

The second study, in collaboration with Drs. Christian Brander and David Scadden of Harvard Medical School, is taking place in Durban, South Africa. The objectives of this community-based, cross-sectional study are to determine the prevalence and determinants of HHV-8 among 480 young children and their primary caregivers, and the prevalence of specific childrearing practices that promote the passing of saliva from caregivers, including mothers, fathers, and siblings, to young children (n=800 caregivers).

Data collected in these two studies will serve as the basis to examine incident HHV-8 infection among infants and children, with a focus on their mothers and other family members as the principal transmitters of infection. Our work in sub-Saharan Africa has an extensive mentoring component for U.S. trainees (Ms. Graves, Graduate Student, and Dr. Butler, Post-doctoral Fellow) and a training component for foreign scholars (Drs. Mosam and Dawood of the Nelson Mandela School of Medicine at the University of KwaZulu-Natal in Durban, South Africa).