SEXUALLY TRANSMITTED INFECTIONS, HIV/AIDS

WHAT'S NEW IN STIS IN HIV INFECTED PERSONS.

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Epidemiologic studies have indicated a strong association between the acquisition of HIV and other sexually transmitted infections (STIs). Herpes simplex virus type 2 (HSV-2) shedding is associated with increased risk for acquiring HIV, and the risk ratio of HIV acquisition for a person with genital herpes is enhanced from 2 to 4 when compared with a person without genital herpes. Potentially 50% of new HIV infections are considered to be attributable or worsened by HSV-2 infection. The prevalence of HSV-2 is high among HIV-infected persons and HSV-2 infection increases the HIV load, the risk of HIV-1 transmission by 2-fold, and the rate of HIV-1 disease progression.
To date, it is not fully understood whether the time of infection is a variable influencing the risk of HSV-2 acquisition and whether such knowledge can facilitate strategies for prevention of the disease. To determine whether the time of infection affects the outcome of HSV-2 pathology, we used an HSV-2 cutaneous infection model. Wild-type mice entrained to 12-hour light/12-hour dark conditions (the light was turned on at 6 AM, which was Zeitgeber time [ZT] 0, and the light was turned off at 6 PM, which was ZT12) were intradermally infected with HSV-2 either at 12:00 AM (rest phase; ZT6) or at 12:00 PM (active phase; ZT18). We observed that the survival rates, clinical scores, and lesional scores were less severe in mice infected at ZT6 than at ZT18. Notably, the viral titers in the skin 1 day after infection significantly decreased in mice infected at ZT6 in comparison with those at ZT18. The degree of the host innate immune response was also less severe in the skin of mice infected at ZT6 than those at ZT18 as judged by expression of inflammatory cytokines and antimicrobial peptides. In addition, the time-of-day dependent variation in the severity of cutaneous HSV-2 infection was preserved in RAG2-deficient mice suggesting that acquired immunity does not play a role in the temporal variations of HSV-2 infection.
The circadian clock consisting of interlocked transcriptional-translational feedback loops of several clock genes drive daily rhythms in physiological processes in various organs or tissues including the skin. To gain a mechanistic insight how the time of infection affected the outcome of HSV-2 pathology, we examined the kinetics of the HSV-2 receptor, Nectin1, as well as that of clock genes in the mouse skin under normal conditions. Nectin1 mRNA and protein expression in the mouse skin was higher at ZT18 than at ZT6 under normal conditions, suggesting that there is a time-of-day-dependent variation in Nectin1 expression in the skin, which may be associated with temporal variations of cutaneous HSV-2 infection. Indeed, we found that clock genes In summary, the current results suggest that the time of

infection is a variable influencing the outcome of HSV-2 pathology, in association with circadian expression of the HSV-2 receptor Nectin1 in the skin that is likely controlled by the molecular clock.