

# Varicella-zoster Virus in the Saliva of Patients with Herpes Zoster



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Varicella-zoster virus (VZV) is the etiologic agent of two diseases, varicella (chickenpox) and zoster (shingles). Varicella typically results from the first exposure to VZV and most commonly is a disease in young children. After the chickenpox resolves, the virus becomes latent in ganglia along the entire neuraxis. Zoster is most commonly a disease of adults. As the cell-mediated immunity (CMI) to VZV declines, usually decades after initial exposure to VZV, the virus reactivates to produce shingles (figure 1). We completed a set of studies to evaluate CMI and viral reactivation in astronauts during flight.

Previous studies demonstrated declines in CMI as well as innate immunity in astronauts. Our initial study of astronauts examined their saliva to determine whether space-flight-associated factors decreased CMI enough to allow VZV reactivation and subsequent shedding in saliva. We used a polymerase chain reaction assay to detect VZV deoxyribonucleic acid (DNA).

Astronauts on a shuttle mission reactivated VZV and shed the virus in saliva. No symptoms attributable to VZV reactivation occurred, but reactivation of the VZV and other latent viruses serves as a sensitive biomarker for decreased CMI.

This astronaut study led directly to a clinical study of zoster patients. The objective was to determine whether zoster patients shed VZV in saliva. Fifty-four patients with

herpes zoster were treated with valacyclovir. On treatment days 1, 8, and 15, we scored pain and examined saliva for VZV DNA. We found VZV DNA in every patient the day treatment started; the virus later disappeared in 82% of the patients. This provided a positive correlation between the presence of VZV DNA and pain and between VZV DNA copy number and pain ( $P < 0.0005$ ). We found VZV DNA in one patient before rash and in four patients after pain resolved; it was not present in any of six subjects with chronic pain or in the 14 healthy subjects.

This was the first large study that demonstrated the presence of VZV in saliva of shingles patients. More importantly, it showed the presence and amount of VZV in saliva correlated with clinical disease; that is, as the symptoms (e.g., pain) dissipated and lesions healed, the VZV in the patients' saliva disappeared. It appears that VZV reactivates during periods of decreased immunity and is shed in saliva prior to rash formation. In one patient, pain preceded rash. After we detected VZV DNA in both a patient's saliva and plasma, that patient's physician treated her immediately with oral valacyclovir. This resulted in a significant decrease in pain coinciding with the disappearance of VZV DNA in her saliva and plasma.

An early clinical sign of impending shingles is pain in one or two dermatomes prior to the appearance of the zoster rash. Early indications are that VZV appears in saliva during this prodromal period. Detection of VZV allows for early diagnosis and rapid intervention therapy. Rapid treatment limits nerve damage.

This study led to the development of a rapid test for VZV in saliva that can be conducted in a physician's office in fewer than 30 minutes. In addition to shingles applications, the test is potentially useful in the diagnosis of neurological disease produced by VZV without rash. In this study, we demonstrated the practical application of NASA-developed technology to everyday life.

Patent application no. 61/087,04 was filed on August 8, 2009 under *Saliva assay for rapid identification of VZV*.



**Fig. 1.** Patient with varicella-zoster virus.