Space Life Sciences Research Highlights

Research on Latent Virus Reactivation Helps Keep Astronauts—and the Public—Healthy

The eight herpesviruses that infect humans can hide within cells for decades after the virus first made a person sick. Later in life, these viruses can cause diseases such as shingles, ocular lesions, meningitis, and tumors in some cases. NASA-funded research into this reactivation has not only identified a useful biomarker for astronaut immune status but is also helping to improve health for people on the ground.

More than 90 percent of the adult population worldwide is infected with a latent herpesvirus. When these viruses first infect a person, they may cause diseases such as mononucleosis and chicken pox. After a person recovers, the virus enters a dormant state in the body and can stay there for years, or even the rest of the person's life, without producing any symptoms.

Usually those viruses stay locked within a person's cells, but sometimes they reactivate. For example, shingles (zoster) occurs when the latent varicella-zoster virus (VZV) that causes chicken pox reactivates later in life. This is very different than what happens with the flu. "With influenza, you feel really bad for a week or 10 days, and then the virus is eradicated," notes Duane Pierson, chief of microbiology at NASA's Johnson Space Center (JSC).

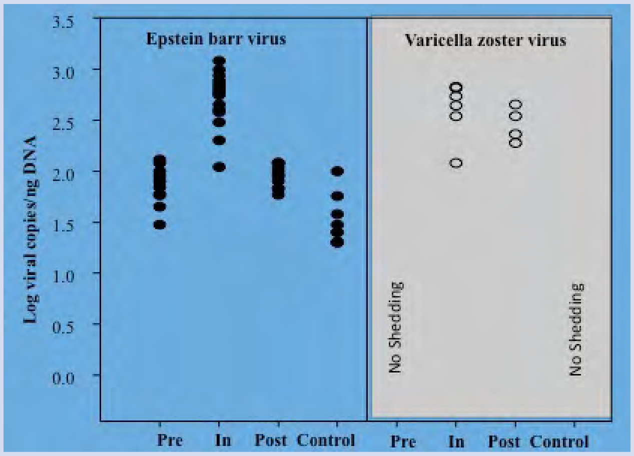
One of the more striking results of studies of human-associated microbes in space is that some latent viruses tend to reactivate in astronauts at a much higher rate while they are in orbit than when on Earth. The mammalian immune system is sensitive to physical stress on the body. As astronauts float through the International Space Station (ISS), their lives, at first glance, may seem to be peaceful. But spaceflight is a uniquely stressful environment. Astronauts will experience increases in G-forces during launch and landing, and weightlessness while in orbit. They may have to deal with stressors such as sleep deprivation or psychosocial stress, while the body copes with extra radiation. All this affects the immune system and may make astronauts more susceptible to disease, note Pierson and his colleague Satish Mehta, a senior scientist at JSC. "When the immune system is compromised due to stresses associated with spaceflight or some other unknown reasons, then those viruses reactivate," Mehta says. This can be a problem because the person may develop disease. Even if they do not, since their bodies are now generating and releasing (shedding) virus copies into the environment, those viruses can infect other unprotected people.

Viruses That Linger

There are eight herpesviruses that can infect humans and hide in their cells. Some of these viruses are very familiar, such as Herpes Simplex Virus (HSV) 1 and 2, which cause oral (cold sores) and genital herpes, respectively. Epstein-Barr virus (EBV), which causes mononucleosis, can spark the development of lymphoma or tumors when reactivated. And the reactivation of VZV causes about 1 million U.S. cases annually of the painful blisters known as shingles, with 100,000 to 200,000 experiencing a debilitating condition known as post-herpetic neuralgia that can last for years, according to the U.S. Centers for Disease Control and Prevention.

Satish Mehta (left) and Duane Pierson (right) of the NASA Johnson Space Center have found that some herpesviruses reactivate in astronauts at a higher rate when they are in orbit.

What is particularly intriguing is that although few astronauts have developed shingles or any of these other conditions before and during spaceflight, Pierson and Mehta have found evidence that latent viruses often do get reactivated when astronauts are in space, causing them to shed infectious, or "live," viruses at an increased rate. The researchers looked for copies of DNA from several herpesviruses—including EBV and VZV—in the blood, saliva, and urine of 17 astronauts. Both EBV and VZV were



Astronauts tended to shed more copies of EBV and ZVZ during spaceflight than they did before or after going into space.

elevated during flight but returned to normal levels within 30 days after return to Earth, Mehta, Pierson, and colleagues reported in the October 2014 issue of *Brain, Behavior, and Immunity*. These astronauts exhibited few other signs that their immune systems had been compromised by the trip to space, and they were not sick. However, they were shedding copies of the viruses into the ISS environment.

To examine a person's immune system on Earth, scientists use a laser-based technology called flow cytometry. But that isn't available on the ISS. Furthermore, measuring a person's immune status before and after their trip to space doesn't provide the full picture of their health while in microgravity. "The problem is there's a lot of stress on launch, a lot of stress on reentry, and it may not represent what was going on in the middle of a six-month mission," says Pierson. So Pierson and Mehta developed an approach to study immune-system status in space environments using latent virus reactivation as a biomarker that is quicker than the more intense, and time-consuming, studies that can be done on the ground.

However, latent virus reactivation is not just a biomarker of immune system status; this process can spread viruses and cause diseases like shingles, so knowing when shedding is occurring is critical. As a result, the method developed by Pierson and Mehta can not only be used in the future to keep astronauts healthy but may also benefit people here on Earth. That's because detecting viral DNA in saliva at an early stage of disease can lessen disease severity and duration of pain and reduce the probability of development of post-herpetic neuralgia and other medical complications.

Early Detection of Shingles

Monitoring viral shedding can give early notice of a disease outbreak and allow prompt treatment. And while shingles or other complications might be manageable on a short-term flight, "if you're on the way to Mars, that could be really problematic," Pierson says. "It could result in a crew member unable to perform some of their duties." Early detection of the disease could help to mitigate that.

Mehta and Pierson have worked to make herpesvirus detection even easier. For instance, a shingles diagnosis is currently based on the presence of a rash, but many of the disease's most serious complications, such as post-herpetic neuralgia and ocular disorders, can develop without being accompanied by any visual changes to the skin. Mehta, though, can detect the presence of active VZV in a sample of saliva, easily obtained with a cotton/synthetic roll. Once a diagnosis of shingles is confirmed, a doctor can prescribe an antiviral medication. "When that happens, the pain begins to subside and then the viruses in the saliva begin to disappear," Pierson notes.

"This can also help if someone is misdiagnosed," Mehta says. He has identified cases in which a doctor has diagnosed shingles but no viral DNA was present in the patient's saliva. "That physician had to agree with our diagnosis that this was not a shingles case, so the treatment had to be changed." The NASA scientists have also helped to diagnose chicken pox in adults.

Mehta and Pierson now work with local physicians to help diagnose cases of shingles and other viral diseases early. "Our job is to do what we can in microbiology to protect the health of the ISS crew and to protect the integrity of the space station," Pierson says, but that can also lead to benefits for those of us who dwell on Earth.

Further Reading

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