

## **CHRONIC FATIGUE SYNDROME LINKED TO HHV-6 VIRUS**

*International Conference on Chronic Fatigue Points to  
Low-grade Viral Infections in Brain*

**February 22, 2005** – The HHV-6 Foundation, an association formed to raise awareness, funding and further research for human herpesvirus 6 (HHV-6), has today announced that some cases of chronic fatigue syndrome (CFS) may be linked to human herpesvirus 6 A variant (HHV-6A). The announcement comes on the heels of the International Fatigue Conference on Fatigue Science that was held in Japan on February 9-11. The conference was attended by some 200 scientists from around the world.

Studies examining the role of the virus in CFS have had conflicting results over the years. The HHV-6 virus was discovered in the late 80's. Although the B variant is very common – over 95% of the population has had it – and causes roseola in infants, the A variant is less common. The A variant has been linked to CFS and multiple sclerosis (MS) and may hasten the progression of HIV. Dr. Ablashi reported that when the correct testing method is used, there is a strong association between HHV-6 and CFS.

Dr. Dharam Ablashi, co-discoverer of the virus and scientific director of the HHV-6 Foundation said, “There is good reason that it has taken a long time to build a case for this virus playing a role in chronic fatigue – it's very difficult to find. The virus is ‘neurotropic’ meaning it prefers to live in the brain tissue. It is quite possible to find a significant infection in the brain tissue, but no virus in the serum by DNA testing.”

Dr. Daniel Peterson, a leading CFS clinician from Sierra Internal Medicine in Nevada, supported this finding. He performed spinal taps on patients with abnormal MRI or severe problems with cognitive functioning and found active HHV-6A virus in the spinal fluid of 20% of those patients. Twenty nine percent of these patients were positive at least once in the serum, and he found many patients who were positive in the spinal fluid but not the blood. Warned Peterson, “Just because you can't find it in the blood doesn't mean it isn't there.”

“Our primary objective at the moment is to get a test on the market that will be a sensitive indicator of active infection,” said Kristin Loomis, executive director of HHV-6 Foundation. “The evidence presented at the conference will go a long way toward dispelling the notion, still held by some physicians, that CFS is purely psychiatric.”

There was a great deal of evidence presented at the conference in support of an infectious cause of CFS. Dr. Takeshi Sairenji of Tottori University showed evidence that 60% of CFS patients vs. 11% of controls had evidence of chronic activated antiviral pathways. He suggested that chronic fatigue might be caused by interferon from viral infections such as HHV-6, Epstein Barr virus and Borna virus.

Dr. Peterson has been treating some of his most severe cases with intravenous antiviral therapy and the majority has responded. He does not tell them they have CFS; he tells them they have HHV-6A subacute encephalopathy. Others have begun calling it the Peterson Syndrome.

- MORE -

For additional information on research findings and where to get tested, got to [www.hhv-6foundation.org](http://www.hhv-6foundation.org).

### **About HHV-6 Foundation**

The HHV-6 Foundation sponsors research on the role of HHV-6 in chronic fatigue syndrome, multiple sclerosis, HIV, epilepsy and other conditions. The Foundation has a Scientific Advisory Board that includes the world's top experts in HHV-6 and is funding basic research in this field. The Foundation is supported through private donations. For more information on the HHV-6 Foundation, visit [www.hhv-6foundation.org](http://www.hhv-6foundation.org) or call 805-969-1174.

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## **ADDENDUM**

**Dan Peterson, MD**  
**Sierra Internal Medicine, Incline Village, Nevada**  
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Dr. Peterson found HHV-6A in 29% of the serum and in 20% of the spinal fluid of his patients with prominent CNS symptoms: neurocognitive problems, headaches, paresthesias or autonomic dysfunction. Of those with virus in the spinal fluid, the blood tests were negative 40% of the time. This means many physicians get false negative results when they test for HHV-6 in the serum.

Peterson tested 430 patients by PCR or rapid culture, and found 126 were positive at least once. He performed 145 spinal taps on patients with an abnormal MRI or severe problems with cognitive functioning. Peterson found one case each of EBV and CMV and 27 cases of HHV-6, all variant A. He has been treating them with intravenous antiviral therapy and the majority has responded. Peterson has had success using Ampligen, an antiviral that is currently in clinical trials, and cidofovir, an antiviral approved for CMV retinitis.

**Dharam Ablashi, MD**  
**Scientific Director, HHV-6 Foundation**  
**302-947-9634**

Dr. Ablashi reported that when studies used the correct testing method, over 80% of the studies showed a strong association between HHV-6 and CFS.

“When you look only at the studies that tested for active (vs. latent) virus in CFS patients, then 10 out of 12 showed a strong positive association between HHV-6A infection and CFS”, he said. Ablashi found the same to be true in the studies on MS patients: 29 out of the 37 studies on MS and HHV-6 showed a positive association. Many of the early studies were done on whole blood, a technique that picks up latent virus, leaving the results muddled. The best tests are those that only pick up active virus – tests done on plasma, serum or spinal fluid with no cells. The problem is that although these are the only tests that can indicate active infection, they aren’t very sensitive.

“There is a good reason why it has taken a long time to build a case for this virus playing a role in chronic fatigue - this is a very difficult virus to find,” said Ablashi. “The virus is ‘neurotropic’ meaning it prefers to live in the brain tissue. “It is quite frequent that a patient might have a significant infection in the brain tissue, but no virus evident in the serum by PCR.”

**Takeshi Sairenji, MD**  
**Department of Biomedical Sciences, Tottori University, Tottori, Japan**

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Dr. Sairenji showed evidence that 60% of CFS patients vs. 11% of controls had evidence of chronic activated antiviral pathways. He suggested that chronic fatigue might be caused by interferon from viral infections such as HHV-6, Epstein Barr Virus and Borna virus.

Sairenji's study supports the previous work of Dr. Kenneth De Meirleir of Brussels and the scientists associated with RED Laboratories who have found similar distinct physical abnormalities among CFS patients.

**Kenneth De Meirleir**

**Department of Human Physiology, Vrije Universiteit Brussel, Brussels, Belgium**  
**de.meirleir@pandora.be**

Dr. Kenneth DeMeirleir, who has published similar findings on elevated antiviral pathways, said that these abnormalities result in the inactivation of the thyroid receptors – so that CFS patients are functionally hypothyroid even though their lab results may appear normal. He reported that these abnormalities also cause an increased sensitivity to heavy metals such as nickel and mercury, as well as a sluggish cortisol response.

**Kazuyoshi Ikuta, MD**

**Research Institute for Microbial Diseases, Department of Virology, Osaka University,**  
**Osaka, Japan**  
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Dr. Ikuta reported his group found a higher prevalence of Borna virus antibodies in both psychiatric and CFS patients compared to controls. He demonstrated that mice injected with Borna virus developed low-grade Borna viral infections in the glial cells of the brain. This low-grade infection disrupted neuronal functioncaus the mice to behave abnormally.

**Abbijit Chaudhuri, MD**

**Division of Clinical Neurosciences and Molecular Pathology, University of Glasgow,**  
**Scotland, UK**  
**Ac54@udcf.gla.ac.uk**

Dr. Chaudhuri, a neurologist from Glasgow, explained that one way that poorly performing glial cells cause fatigue is by altering ion channels and creating a 'channelopathy.' He believes that there are many triggers for CFS, but they ultimately all end up with a common pathway in creating fatigue: a disruption of the ion channels.

Chadhuri used as an example, chronic fatigue caused by ciguatera fish poisoning. The ciguatera toxins block the sodium ion channels, which result in too much extra-cellular potassium, which in turn creates fatigue. Glial cells, which are supposed to buffer the amount of potassium

released from the neurons, do not function well when they are infected with virus. HHV-6A virus actively reproduces inside the brain's glial cells, while the B variant simply smolders – but both strains induce inflammatory cytokines.

**Kazuhiro Kondo, MD**  
**Chairman of the Department of Microbiology, Jikei University School of Medicine, Tokyo, Japan**  
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Dr. Kondo found that 88% of Japanese workers expressed HHV-6 B virus in their saliva when they were stressed just before the holidays, but found it in only 24% after the holidays when the same workers were refreshed.

There is almost no variant HHV-6 A in Japan so his studies were based on the B variant, which according to Dr. Kondo is far less pathogenic than the A variant but much quicker to activate.

**Norihiro Sadato, MD**  
**Osaka University School of Medicine, Osaka, Japan**  
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Dr. Sadato used advanced, quantitative MRI techniques to examine 16 CFS patients and 49 controls and found marked differences. CFS patients had reduced gray-matter volume in the prefrontal cortex and the severity of the atrophy related to the severity of fatigue in the patients. . Furthermore, when the dysfunctional areas of the brain were pinpointed, they turned out to be the centers of the brain that control emotion, executive functioning and motivation. Sadato noted that these results were consistent with previous reports of abnormal acetyl-L-carnitine uptake in the pre-frontal cortex in CFS patients. These abnormalities are similar to those reported in MS patients, who also have a high incidence of MS.

**Benjamin Natelson, MD**  
**Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark, NJ**  
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Dr. Natelson, a neurologist who runs a large CFS clinic in New Jersey, was among the speakers presenting evidence of brain inflammation due to encephalopathy. Natelson found evidence of inflammation in the spinal fluid in 30% of his CFS patients. Natelson concluded that this study supports the hypothesis that some CFS patients have a brain disease.

**Gundrun Lange, MD**  
**Department of Radiology, UMDNJ-New Jersey Medical School, Newark, NJ**  
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Dr. Lange declared chronic fatigue to be a ‘brain disease’. Lange used functional neuroimaging to examine verbal working memory in CFS patients and found dramatic differences in performance that could not be explained by mood or anxiety. The neural networks in CFS patients, as measured by the blood oxygen signals, worked much harder than non-CFS patients when given the same task to complete. Lange said this would explain the subjective reports of neurocognitive difficulties in information processing that are a common complaint among CFS patients.

**Nancy Pederson, MD**  
**Department of Medical Epidemiology and Biostatistics**  
**Karolinska Institute, Stockholm, Sweden**

Dr. Pederson reviewed telephone interview data from 12,407 sets of twins enrolled in the Swedish Twin Registry and found that genetic factors in CFS were “modest”, explaining only about 35% of the disease. This suggests to Pederson that environmental triggers, such as toxins, stress and viruses, are important to the pathogenesis of CFS.