# EPSTEIN-BARR-VIRUS: A CAUSATIVE FACTOR IN CHRONIC PAIN CONDITIONS

By Forest Tennant DrPH, MPH, MD

PREPARED FOR PAIN MEDICINE NEWS

APRIL 2024

When most people hear about the Epstein-Barr virus (EBV), they may recall its reputation as the rather harmless "kissing disease" known as mononucleosis. To the surprise of many, this previously unheralded virus has recently emerged as a cause of some cancers and painful disorders.

It is now clear that EBV must be contained and suppressed in order to relieve the pain and suffering of many persons with chronic pain. This column is an introduction to the critical involvement of EBV with several chronic pain conditions.

The Epstein-Barr virus is named after Drs. Anthony Epstein and Yvonne Barr. In 1964, they discovered the virus after they found it in a cancer common in Africa called Burkitt's Lymphoma. Since that time, EBV has been found to cause other cancers including nasopharyngeal, gastric, Hodgkin's lymphoma, and leukemia. Some estimate that EBV causes about 200,000 cancers a year.
About three years after Epstein and Barr discovered EBV, it was found to be the cause of infectuous mononucleosis, which is known to trigger autoimmune complications. Autoimmunity is simply defined as some element in the body that attacks, erodes, and destroys tissue.

In 1968, this author reported that mononucleosis could cause glomerulonephritis, an autoimmune renal disease. Over the ensuing decades, EBV has also been associated with other autoimmune disorders, including hepatitis, rheumatoid arthritis, fibromyalgia, systemic lupus, and Sjogren's syndrome.

**EPSTEIN-BARR VIRUS**

In 2018, a seminal study documented that EBV could cause a number of painful medical conditions by activating specific genes. Dr. John Harley and colleagues at Cincinnati Children's Hospital Medical Center, with funding from the National Institutes of Health, found that a viral protein called Epstein-Barr nuclear analog 2 (EBNA 2) binds to the deoxyribonucleic acid (DNA) of genes that promote autoimmunity and some chronic pain conditions.

The pain conditions that Harley and his colleagues associated with EBV are multiple sclerosis, rheumatoid arthritis, celiac disease, type 1 diabetes, inflammatory bowel disease, thyroiditis, and

juvenile arthritis. Subsequent studies added Sjogren's syndrome, mixed connective tissue disease, and polymyositis to the list of EBV autoimmune conditions.

The Harley research is compelling. We urgently need clinical studies of EBV in severe chronic pain patients to help develop new diagnostic, prevention, and treatment measures. To this end, I've chosen to study the EBV relationship to painful spine and connective tissue diseases, especially adhesive arachnoiditis (AA) and Ehlers-Danlos syndrome (EDS). These conditions are considered intractable pain conditions in clinical pain practice.

So far, we have collected EBV laboratory test results from over 80 persons with confirmed AA. *Every case* has demonstrated abnormally high levels of EBV IgG antibodies, which suggests the presence of autoimmunity and the possible invasion of brain and spinal tissue by the virus.

Every patient with high IgG antibody levels also has herniated discs, and the majority have hypermobile EDS. Prior to developing AA, all had conditions associated with autoimmunity, such as fibromyalgia and small fiber neuropathy. All of them now have intractable pain.

**How It Begins**

Patients and clinicians concerned about chronic pain need to understand the basics of how EBV causes and aggravates chronic pain conditions.

EBV is a member of the herpes virus family, which includes the other herpes viruses and cytomegalovirus. It is a natural, lifelong parasite that usually infects children before the age of two.

When EBV first enters the body, it is an “active” virus that may cause a cold, sinusitis, bronchitis, or possibly even go unnoticed. Infants and young children often have the “sniffles” and it could be mistaken as a simple cold. Some children who initially become infected with EBV later develop mononucleosis in their teenage or young adult life.

After the initial infection, EBV settles into one’s lymphocytes and lining of the throat and nasal cavity to remain for life. Under normal physiologic circumstances, it is a latent or dormant parasite that does no harm.

Over 95% of adults will test positive for low levels of IgG antibodies, decades after their initial contact with EBV during childhood. When chronic pain patients are tested, autoimmunity is suspected if IgG antibodies are above normal levels found in the great majority of adults.

Once EBV has settled into lymphocytes or the throat lining and becomes dormant, it is living a harmless, symbiotic, parasitic life with its human host. It will remain in this state, unless the body undergoes some kind of stress, usually trauma or an infection, that lowers or degrades the body's innate or natural immunologic protection systems.

At this time, the virus may vacate its dormant or latent state to begin what is called a "lytic" or duplicative state. The term used to indicate this state is "reactivation," meaning that the virus is again active, and attacking and invading new tissues.

Once reactivated, EBV may create an autoimmune state by altering genes or by developing what is called an auto-antibody that will attack tissues. In either case, an autoimmune state has been created that attacks normal tissues to produce inflammation, adhesions, scarring, and pain.

Lymphocytes infected with reactivated EBV may enter any number of tissues. They may cross the blood brain barrier, enter the spinal cord and brain, and attack tissues such as the cauda equina, arachnoid membrane, intervertebral discs, and glial cells. This is the pathologic process in which EBV reactivation may cause chronic pain.

It is likely that entry and invasion of spinal canal and brain tissues may be responsible for the autoimmune manifestations seen after a stroke, head trauma, or complex regional pain syndrome (CRPS). EBV may also be a cause of centralized pain that is associated with over-sensitization, hyperalgesia, and intractable pain. There are reports that such common chronic pain conditions as fibromyalgia, small fiber neuropathy, and some arthropathies are caused by EBV autoimmunity.

This article's major intent is to inform all concerned parties that deal with chronic pain that EBV is not just some virus that causes the "kissing disease." It is a new revelation that compels an understanding and awareness that has the distinct potential to improve the plight of chronic pain patients.

Laboratories and clinical researchers, including this author, are scurrying to identify more diagnostic, treatment, and preventive measures for EBV-caused autoimmunity. I'm pleased to report that our EBV project has been able to identify some initial testing and treatment measures which appear to be effective and a good start in dealing with EBV autoimmunity. We will share our findings in future articles.

*Forest Tennant, MD, DrPH, is retired from clinical practice but continues his research on the treatment of intractable pain and arachnoiditis. Readers interested in learning more about this research should visit the Tennant Foundation's website, Arachnoiditis Hope. You can subscribe to its bulletins here.*

*The Tennant Foundation gives financial support to Pain News Network and sponsors PNN's Patient Resources section.*