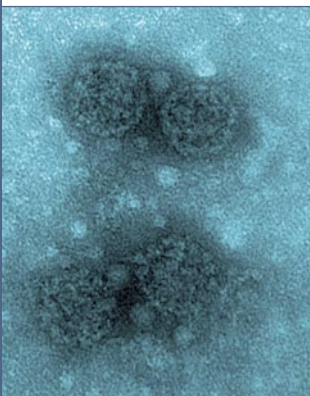


# JC Virus Overview

## ABOUT THE VIRUS

The JC virus (JCV) is a member of the Polyomaviridae family, which consists of small, nonenveloped viruses with a closed, circular double-stranded DNA genome. Polyomaviruses are ubiquitous in nature and can be isolated from a number of species. The human polyomaviruses were first isolated in 1971 and named JC and BK after the initials of the patients in which they were first discovered. JCV was isolated from the brain tissue of a patient with progressive multifocal leukoencephalopathy (PML). BKV and JCV share 75% homology at the nucleotide sequence level. JCV is the etiologic agent of PML, which only occurs in immunocompromised hosts.



Polyomavirus viewed at 340,000x (negative staining) by transmission electron micrograph. Image courtesy of UMICH.

## CLINICAL MANIFESTATIONS

An estimated 60-80% of adults in Europe and the United States have antibodies to JCV. JCV and BKV are believed to circulate independently. JCV appears to be acquired later in childhood than BKV, at 10-14 years versus 3-4 years, respectively. Evidence is unclear regarding the transmission of JCV and the course of events during primary infection. Currently, there is not an acute disease associated with JCV primary infection. It is proposed that JCV establishes a latent infection in the kidney following a primary infection, similar to BKV. Some evidence indicates latency also develops in the central nervous system. In-situ DNA hybridization has demonstrated JCV in B lymphocytes, bone marrow, lung, spleen, lymph node tissue and tonsillar tissue.

Progressive multifocal leukoencephalopathy (PML) is a rapidly progressing, extremely debilitating demyelination disease caused by infection of the central nervous system with JCV. It usually occurs in patients with diminished T cell function. PML is characterized by neurological deficits that progress rapidly, including hemiparesis, cognitive disturbance, visual field deficits, ataxia, aphasia, cranial nerve deficits and sensory deficits. Patients who have PML typically deteriorate rapidly and death commonly occurs within 6 months of

diagnosis, however, a subset of patients will experience fluctuating symptomology over a 2-3 year period.

PML is a rare disease that almost always occurs in the setting of significant immunosuppression, more specifically, in the setting of abnormalities of cell-mediated immunity. Prior to the AIDS epidemic, lymphoproliferative disorders were the most common predisposing illnesses accounting for described cases of PML. Only 230 cases were described between 1958 and 1984. The AIDS pandemic dramatically changed the demography of PML. Prior to the adoption of highly active antiretroviral therapy (HAART) in 1996, approximately 5% of all HIV infected patients developed PML. More recently, PML has been described in a few patients receiving certain monoclonal antibodies, natalizumab and rituximab, for the treatment of several auto-immune disorders and B-cell lymphomas, respectively. The virus' exact mechanism of entry into the CNS is not understood at this time.

There are a few reported cases in the literature of JCV causing nephropathy in renal transplant patients, much like BKV. However, this appears to be unusual.

Several studies have demonstrated that the virus is often present in the urine of up to 70% of the subjects studied, but generally not found in blood, saliva, nasopharyngeal aspirates or throat washings of either healthy subjects or HIV patients. In the case of PML patients, the virus appears to be present in the blood in very low titers, but present in CSF in high titers.

## LABORATORY DIAGNOSIS

The presence of JCV is detectable using a sensitive and specific quantitative real-time PCR assay, which can be performed on a variety of specimen types, such as CSF, urine, blood and organ biopsies. However, it is important to ascertain if the molecular assay being used is specific to JCV or if it cross reacts with BKV. The two viruses share a high level of homology and many molecular assays are unable to differentiate between the two. The ViraCor JCV assay was carefully developed to be specific for JCV and not cross react with BKV.

## TREATMENT

Currently, there is not a specific antiviral therapy proven effective for JCV. Current treatment of immunocompromised patients consists of restoring cell-mediated immunity to the greatest extent possible. Cidofovir is currently being studied as a treatment option for transplant patients, and cytarabine can be used in the treatment of PML, although there is conflicting data regarding the efficacy of the latter.

### Selected References

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