CONDITION

Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencephalopathy is a serious brain infection caused by JC virus when immune defences are weakened.

WHAT IT IS
JC virus infection damaging the brain's white matter

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Weakness, vision changes, speech problems, thinking changes

WHAT CAUSES IT
Infection during severe immune suppression

HOW IT IS DIAGNOSED
Brain MRI and JC virus testing of spinal fluid

MAIN TREATMENT
Restoring immune function and supportive rehabilitation

CAN IT BE CURED?
No - immune recovery may stop progression

IS IT AN EMERGENCY?
Yes - suspected symptoms need urgent neurological assessment

LONG-TERM OUTLOOK
Often serious; outcomes improve when immune function recovers

Overview

Progressive multifocal leukoencephalopathy, usually called PML, is an uncommon but serious condition affecting the brain. It is caused by the JC virus, also called John Cunningham virus.

Many people are exposed to JC virus without knowing it. The virus can remain inactive in the body for years and usually causes no symptoms. PML can develop if weakened immune defences allow the virus to become active in the brain.

The virus damages cells that make myelin. Myelin is the protective covering around nerve fibres. When myelin is lost, messages can no longer travel normally through affected parts of the brain. This can change movement, vision, speech, coordination, behaviour or thinking.

"Progressive" means symptoms tend to worsen over time without effective immune recovery.

"Multifocal" means more than one area may be affected. "Leukoencephalopathy" means damage to the brain's white matter, which contains many myelin-covered nerve fibres.

PML is not a brain tumour, an inherited condition or a form of dementia. It is also not generally spread through ordinary contact with someone who has it.

Symptoms

Symptoms depend on which areas of the brain are affected. They often develop over days to weeks and become steadily more noticeable. Different symptoms may appear as additional areas become involved.

Possible symptoms include:

Symptoms may begin subtly. Someone might repeatedly drop objects, bump into things on one side, struggle to find familiar words or become unusually confused.

These symptoms are not specific to PML. Stroke, medication effects, other infections, multiple sclerosis and several other conditions can cause similar problems. A medical assessment is needed to find the cause.

- Weakness, heaviness or reduced control on one side of the body
- Trouble walking, poor balance or clumsiness
- Blurred vision, loss of part of the visual field or other visual changes
- Difficulty speaking, understanding language, reading or writing
- Problems with attention, memory, planning or decision-making
- Changes in personality, mood or behaviour
- Numbness or altered sensation
- Seizures

Causes and risk factors

PML occurs when JC virus becomes active in a person whose immune system cannot control it effectively. Having evidence of past JC virus exposure does not mean that PML will develop. Most exposed people never develop it.

The main risk factor is significant weakening or alteration of the immune system. Situations associated with PML include:

PML has been linked to several immune-modifying medicines used for multiple sclerosis, cancers, inflammatory conditions and transplant care. Risk is not the same for every medicine or every person. For some treatments, factors such as previous immune-suppressing treatment, treatment duration and JC virus antibody results help specialists assess risk.

Do not stop an immune-modifying medicine because of concern about PML without speaking to the team that prescribed it. Suddenly stopping treatment can allow the original condition to worsen, and some medicines need a planned transition.

- Advanced HIV infection, especially when it is untreated
- Certain blood cancers, such as leukaemia or lymphoma
- Stem cell or organ transplantation
- Some inherited or acquired immune system conditions
- Medicines that suppress or change immune activity

Diagnosis

PML should be assessed by specialists, commonly including a neurologist and a doctor experienced in infections or immune conditions.

The assessment begins with a neurological examination. This checks abilities such as strength, coordination, vision, speech, sensation, memory and attention. The clinician will also review symptoms, immune conditions and current or previous medicines.

A brain MRI is a central part of diagnosis. MRI uses a magnetic field to produce detailed images. PML often causes characteristic areas of damage in the brain's white matter, although scans must be interpreted alongside symptoms and test results.

A lumbar puncture may be performed. This involves taking a small sample of cerebrospinal fluid, the clear fluid surrounding the brain and spinal cord, through a needle in the lower back. A laboratory test called polymerase chain reaction, or PCR, looks for JC virus genetic material in the fluid.

A positive JC virus PCR result together with compatible symptoms and MRI findings can confirm PML without brain surgery. A negative result does not always rule it out, particularly early in the condition or when only a small amount of virus is present. Specialists may repeat the lumbar puncture, use a more sensitive test or follow MRI changes.

Occasionally, a brain biopsy is needed when tests remain unclear. A surgeon removes a small tissue sample for examination. This is usually reserved for situations where confirming the diagnosis will change management and less invasive tests have not provided an answer.

A blood test showing JC virus antibodies indicates previous exposure. By itself, it cannot diagnose active PML.

Treatment and management

There is no antiviral medicine proven to directly eliminate JC virus from the brain. The main treatment approach is to restore enough immune function for the body to control the infection.

For someone with HIV, this usually means starting or optimising antiretroviral therapy. These medicines suppress HIV and allow immune defences to recover.

If PML is associated with an immune-modifying medicine, specialists may stop or adjust that treatment. The plan takes into account how long the medicine remains in the body and the risk of the original condition returning. In selected situations, a procedure that removes medicine from the bloodstream may be considered.

As immunity returns, inflammation can sometimes increase around damaged areas of the brain. This is called immune reconstitution inflammatory syndrome, or PML-IRIS. It may cause new or worsening symptoms even though the immune system is responding to the virus. Specialists use clinical changes and MRI findings to distinguish PML-IRIS from continuing infection. Corticosteroids like prednisone or hydrocortisone may be considered when inflammation is causing serious swelling or deterioration, but they are not routinely used for every case.

Several antiviral like acyclovir or oseltamivir , immune-based and cancer immunotherapy treatments have been studied. None is an established treatment for all people with PML. Experimental options may be discussed at specialist centres when standard immune restoration is not possible or has not worked.

Supportive care is important. Depending on the effects of PML, this may include:

- Physiotherapy for strength, balance and mobility
- Occupational therapy for daily activities and home adaptations
- Speech and language therapy for communication or swallowing
- Treatment for seizures, muscle stiffness, pain or mood symptoms
- Nutrition support and measures to reduce falls or pressure injuries

Complications

Brain damage from PML can leave lasting problems with movement, vision, speech, swallowing or thinking. Some people need help with personal care, communication, transport or managing medicines and finances.

Swallowing difficulty can allow food or fluid to enter the lungs, leading to aspiration pneumonia. Reduced movement can contribute to blood clots, pressure injuries, muscle shortening and loss of physical fitness. Seizures may occur when affected areas are close to the brain's outer surface.

PML-IRIS can cause brain swelling and neurological deterioration during immune recovery. It requires close specialist monitoring because treatment must balance harmful inflammation against the need for an effective immune response.

PML can be fatal, particularly when immune function cannot be restored. Earlier recognition and effective immune recovery offer the best opportunity to stop progression, but they cannot always reverse damage that has already occurred.

Prevention

JC virus exposure usually cannot be prevented, and there is no vaccine against it. PML itself cannot always be prevented when severe immune suppression is necessary or unavoidable.

Risk can sometimes be reduced through careful management of the underlying condition. Effective HIV treatment helps prevent the severe immune suppression associated with PML. Keeping scheduled HIV monitoring appointments is important even when you feel well.

People taking medicines linked to PML may have planned neurological reviews, blood testing or MRI monitoring. For natalizumab, a medicine used for multiple sclerosis, JC virus antibody results may form part of a wider risk assessment. A positive antibody test means previous exposure; it does not mean that you have PML.

Know which new neurological symptoms your treatment team wants reported promptly. Do not delay reporting symptoms until the next routine appointment, and do not stop treatment on your own.

Living with it and what to expect

The course of PML differs according to the areas of brain affected, how quickly it is recognised and whether immune function can recover. Symptoms may continue to worsen for a period after treatment begins because immune recovery takes time.

When the immune system gains control of the infection, MRI changes may stabilise and some abilities may improve. Recovery can continue over months. Nerve rehabilitation often involves repeated practice and adapting tasks around abilities that do not fully return.

Some survivors live independently, while others need ongoing assistance with mobility, communication, personal care or decision-making. Fatigue and slowed thinking can remain important even when physical symptoms are less visible. Home adaptations, mobility equipment and support from family or care services may make daily life safer.

Follow-up commonly includes neurological examinations and repeat MRI scans. The team may also monitor the underlying immune condition, treatment side effects, swallowing, nutrition and seizure risk. Routine appointments are used to track recovery, adjust rehabilitation and plan longer-term support.

Emotional reactions such as fear, frustration, grief or low mood are understandable. Psychological support can help both the person affected and those close to them adjust to changes and uncertainty.

When to get medical help

Seek urgent medical assessment for new or worsening neurological symptoms, especially if you have a weakened immune system or take a medicine associated with PML. Examples include increasing weakness, new visual loss, worsening balance, speech difficulty, confusion or unusual behaviour changes.

Contact the specialist team the same day if symptoms are developing gradually but are clearly new. Do not wait for a routine follow-up appointment.

Call emergency services for:

Routine follow-up is appropriate for stable, previously assessed symptoms, rehabilitation needs and medicine questions. Report changes sooner if function begins to decline.

- Sudden weakness, facial drooping or difficulty speaking, which may be a stroke
- A first seizure or a seizure lasting several minutes
- Loss of consciousness or inability to wake normally
- Severe breathing difficulty or choking
- Rapidly worsening confusion or inability to walk safely

Common questions

Is PML contagious?

PML is not considered contagious through ordinary contact. JC virus is widespread, but exposure usually happens long before PML develops. Living with, touching or caring for someone with PML does not normally place a healthy person at risk of developing the condition.

Does a positive JC virus test mean I have PML?

No. A positive blood antibody test usually means you were exposed to JC virus at some point. It does not show that the virus is damaging the brain. Diagnosis requires neurological assessment, MRI findings and usually testing of cerebrospinal fluid.

Can you recover from PML?

Some people stabilise and regain abilities when their immune system recovers. Improvement may continue for months, often with rehabilitation. Other people have lasting disability, and PML can be fatal. The amount of recovery cannot be predicted from one symptom or test alone.

How quickly does PML progress?

Symptoms commonly develop and worsen over days to weeks, although the pace is not identical for everyone. New problems may appear as different brain areas become affected. Prompt assessment matters because earlier immune restoration may limit further injury.

Can PML come back?

PML can reactivate or progress if immune control remains weak or is lost again. Recurrence appears to be uncommon after sustained immune recovery, but long-term monitoring may still be needed. New neurological symptoms should be assessed rather than assumed to be old damage.

Should I stop my immune-suppressing medicine?

Do not stop it without instructions from the prescribing team unless emergency clinicians advise otherwise. The risks of PML, stopping treatment and allowing the original condition to return must be considered together. New neurological symptoms need urgent assessment so that any change can be planned safely.

Sources



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