

Tests

- Introduction
- Computed tomography (CT) scan
- Magnetic resonance imaging (MRI)
- Electroencephalography (EEG)
- Cerebrospinal fluid (CSF) exam
- Tonsil biopsy
- Brain biopsy
- Autopsy

Introduction

When a diagnosis of Creutzfeldt-Jakob disease (CJD) is suspected, your doctor will likely order a number of tests. These can be helpful to either exclude other neurological diseases or support the CJD diagnosis.

Some of these tests that need to be performed may be frightening or confusing to a patient, so ask your doctor if you, or someone you trust, can be with them during each test. Furthermore, do not be afraid to ask for an explanation if you do not understand why a certain test is being done and what it involves. When you do get the results, keep in mind that test results are only meaningful when correlated with the medical history, particularly symptoms and exam findings.

The following sections describe some of the tests your doctor might order to help make a diagnosis.

Computed tomography (CT) scan

A computerized tomography, or CT, scan is an X-ray technique that produces cross-sectional images of the inside of your body or head. Typical scans last only a few minutes, during which time you should lie still. You may hear some whirring and clicking noises during this test, which is normal. In order to make the CT image, you will be briefly exposed to X-ray radiation, so you might want to confirm with your doctor that it is worth doing the scan. Remember to discuss any concerns you have with your doctor.

A CT scan of the head cannot diagnose prion disease, although sometimes it can diagnose other neurological conditions, such as tumors, strokes or a bleed in the brain. If the CT does not rule out CJD by finding another diagnosis, the next step is most likely a brain MRI. In many circumstances, a brain MRI will be done before or instead of a head CT. Here at UCSF, we order a body CT with and without intravenous contrast on almost all patients with suspected CJD, in order to thoroughly rule out other possible diagnoses, such as a cancer.

Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) uses magnetic fields and radio waves, without any X-rays, to produce images of the inside of your body. It is non-invasive and considered very safe, but some people with metal implants and cardiac pacemakers are unable to have MRI due to the interaction of the magnetic field and radio waves with these devices. Talk to your doctor or the imaging technician if you have any concerns about entering the magnet. Some people find lying in the scanner produces anxiety or claustrophobia because of the tube-like shape or the loud sounds during the scan. Sedation may be available to you if needed, but relaxation techniques like deep breathing, visualization and meditation can also help. Some MRI scanners allow you to listen to music or watch a movie. To get the best pictures, you need to be as still as possible while in the scanner. For people who cannot get a MRI because of a pacemaker, a CT may be performed, although this test cannot diagnose CJD.

We have found brain MRI to be the single most helpful tool for diagnosing CJD. Two types of MRI sequences, Fluid Attenuated Inversion Recovery (FLAIR) and particularly diffusion-weighted imaging

(DWI), typically show abnormalities in the cerebral cortex, striatum and/or thalamus of the brain in people with CJD. The presence and pattern of these abnormalities can support a diagnosis of CJD and may eliminate the need for invasive tests, such as a brain biopsy. For people who might have CJD but can't get a MRI, a brain biopsy may be necessary to make the proper diagnosis.

Electroencephalography (EEG)

An electroencephalogram (EEG) shows patterns of electrical activity produced by your brain as recorded by electrodes placed on your scalp. It is non-invasive and minimally uncomfortable (the electrodes may scratch or itch you and are held in place with a sticky paste). The electrodes do not generate any electricity; they only record electrical activity produced by your brain. You will need to be still with your eyes closed during the 20-40 minute recording in order to get a quality EEG.

The majority (65%) of EEGs from people with sporadic CJD show characteristic abnormalities (spike and wave complexes about once every second) at some point in their disease course; these abnormalities, however, may not appear until late in the disease. Furthermore, the characteristic EEG changes are not specific to CJD, as they are also seen in toxic/metabolic conditions (e.g., severe liver disease) and even rarely in Alzheimer's disease, Lewy Body Disease and Hashimoto's encephalopathy. In most people with CJD, the EEG will just show slowing of brain electrical activity, which is not specific for CJD and occurs in many neurological conditions.

Cerebrospinal fluid (CSF) exam

In all cases of CJD or other rapidly progressive dementia, an examination of your cerebrospinal fluid (CSF - the clear and colorless, watery liquid that surrounds your brain and spinal cord) should be performed. Many different tests may be ordered from the CSF to rule out or investigate the possibility of various conditions. For instance, an elevated white blood cell count in the CSF may suggest a possible infection or inflammatory condition. A doctor collects the CSF by doing a lumbar puncture (spinal tap) in which a very thin needle is gently inserted in your lower back between two vertebrae, the bony structures that make up your spine. The procedure usually is done in a doctor's office and takes about 30-45 minutes, during which time it is important to remain still. Afterwards, drink plenty of fluids to help prevent "lumbar puncture headache." If you have a headache or develop a fever after a lumbar puncture, let your doctor know immediately, as there are things that can be done to make the headache go away.

In people with CJD, the results of the CSF examination are usually normal, with the exception of a slightly increased total protein count. If there is an increased white blood cell count, your doctor should consider other neurological diseases, particularly infections, such as encephalitis.

Although we cannot yet detect prions in the CSF of patients with CJD, detection of elevated levels of the 14-3-3 protein in the CSF has been reported to support a CJD diagnosis in the scientific literature. The UCSF doctors do not feel this test is a very good diagnostic test for CJD because many people with confirmed CJD have a negative or normal result, and many others who do not have CJD, but have other neurological disease, have a positive result. Only half of the patients diagnosed with CJD at UCSF have an elevated 14-3-3 protein. Furthermore, in about 1/3 of patients referred to UCSF with an elevated 14-3-3 protein, UCSF doctors identify another diagnosis, not CJD! In many cases, these other diagnoses are very treatable.

Other CSF proteins, including neuron-specific enolase (NSE) and total tau protein (T-tau), have also been reported to be helpful in diagnosing CJD. UCSF doctors currently are studying the usefulness of these tests for CJD diagnosis, but at present, the medical and scientific community is still debating the use of any of these as a diagnostic test for CJD. So far, the data accumulated through the CJD research group suggests that MRI is a much better test than these CSF markers, but we still recommend ordering these tests as they may indicate that there is rapid injury to nerve cells in the brain.

Tonsil biopsy

A tonsil biopsy is a surgical procedure using a needle or scalpel to remove a small amount of tissue from the tonsil for inspection under a microscope. It helps to identify abnormal cells and growths, but as with any invasive procedure, there are possible risks such as infection and bleeding. This procedure is done in a surgical operating room.

Because variant CJD (vCJD) is the only form of CJD to involve the lymph nodes, spleen, tonsil and appendix, the tonsil biopsy is a diagnostic test for vCJD. We only recommend a tonsil biopsy if vCJD is being considered in the differential diagnosis, as this test is not helpful for any other form of prion disease. A negative tonsil biopsy result, however, does not rule out a diagnosis of vCJD.

For a tonsil biopsy, special precautions to prevent the spread of prions must be taken in the operating room. Usually, the equipment used for the procedure is destroyed by incineration. For more information, please refer your doctor to the [UCSF Infection Control Website](#) .

Brain biopsy

A brain biopsy is a neurosurgical procedure in which a brain surgeon removes a small amount of brain tissue to be examined for the presence of prions (misshapen prion proteins). This procedure is done in the operating room. This invasive procedure carries risk of infection, bleeding or disruption of brain function, although it is generally a safe, well-tolerated procedure. In cases of prion disease, however, the procedure exposes the surgical team to prion infection and special precautions to prevent the spread of prions must be taken in the operating room. Currently, at our institution; all instruments used in the procedure need to be destroyed by incineration after the procedure and cannot be used on another patient. For more information, please refer your doctors to the [UCSF Infection Control Website](#) .

Because of the diagnostic usefulness of diffusion-weighted (DWI) MRI, in most cases of CJD we no longer recommend a brain biopsy. In some cases, in which the diagnosis is still uncertain even after a DWI MRI, brain biopsy may be necessary. The biopsy carries the risks of any invasive procedure, but also the tissue removed for analysis may not always show any prions, even if the person has human prion disease. Although a brain biopsy that is positive for prion disease means that the patient has prion disease, a negative brain biopsy does not rule out prion disease. A brain biopsy in a patient with CJD may be negative for a variety of reasons. In some cases, prion disease is not definitely confirmed until tissue from a brain autopsy is analyzed. Our center consults in many such cases.

Autopsy

The only way to diagnose CJD with absolute certainty is by neuropathological examination either by brain biopsy or at autopsy. For public health and epidemiologic reasons, the [National Prion Disease Pathology Surveillance Center \(NPDPS\)](#) in conjunction with the [US Center for Disease Control and Prevention \(CDC\)](#) strongly encourages families with patients who suffer from prion disease to consider autopsy for their loved one.

A specialized doctor called a neuropathologist conducts a brain autopsy in order to examine the brain tissue to determine a person's cause of death. The procedure can be done in ways to accommodate religious, cultural or personal wishes for funerary customs.

For help in obtaining autopsy for patients with prion disease outside of UCSF, please contact the NPDPS. Patients who participate in UCSF CJD research projects or who are UCSF patients, please contact our [Autopsy Coordinator](#) for more information.