

# DIAGNOSING SPORADIC CREUTZFELDT-JAKOB DISEASE: ACCURACY OF THE 14-3-3 PROTEIN TEST OF THE SPINAL FLUID

This information sheet may help you understand how the 14-3-3 protein test helps in diagnosing sporadic Creutzfeldt-Jakob disease (CJD).

Neurologists from the AAN are doctors who identify and treat diseases of the brain and nervous system. The following evidence-based information\* is provided by experts who carefully reviewed all available scientific studies on accuracy of the 14-3-3 protein test in diagnosing sporadic CJD.

## WHAT IS CJD?

CJD is a rare, progressive brain disorder. In CJD, the nerve cells in the brain break down very quickly. On average, symptoms set in at about age 60 years. Early symptoms include:

- Memory problems
- Behavior/personality changes
- Loss of muscle coordination
- Vision problems
- Insomnia (difficulty falling asleep or staying asleep)
- Depression
- Unusual sensations

As the disease progresses, the person usually develops dementia. This leads to thinking problems that are severe enough to affect the ability to do everyday activities. Other symptoms that may occur later include:

- Involuntary (uncontrolled) movements
- Blindness
- Weakness in the legs and arms
- Inability to speak or move
- Coma (deep state of unconsciousness)
- Pneumonia or other infections

Each year, about 200 people in the United States develop CJD. Worldwide, about one in every one million people per year will develop it. The most common form is sporadic CJD (sCJD). It accounts for about 85 percent of cases. This form is called "sporadic" because it develops in people with no known risk factors.

### WHAT CAUSES CJD? IS IT CONTAGIOUS?

CJD is in a family of brain disorders called "transmissible spongiform encephalopathies." In these disorders, the brain becomes infected. In regard to CJD, the cause is not fully understood. It is thought that a type of protein called a "prion protein" (PrP) causes the disease. The PrP typically is found in the brain and other body organs. When the PrP changes shape suddenly, it becomes a prion. This is an infectious protein that can infect other proteins. As a prion, it then causes other PrPs to change shape and become prions. The prions begin to group together in the brain. Experts believe that these groups of prions cause damage to nerve cells in the brain. However, how this damage occurs is not well understood.

CJD is not spread through the air or through casual contact. It can be spread through contact with the brain tissue or spinal fluid of a person with the disease. Thus, doctors and scientists who come into contact with infected brain tissue or spinal fluid take special safety measures to lessen risk.

### HOW IS SCJD DIAGNOSED?

Diagnosing sCJD can be challenging. sCJD symptoms are similar to those of other nervous system disorders. This makes it hard to know if the person has sCJD or another disorder. Also, there is no single test that can diagnose sCJD reliably. These factors can delay diagnosis, which then delays important disease care and management.

Several tests may be used to rule out other disorders or identify features specific to sCJD. One accurate test is a brain biopsy. In a biopsy, a small piece of brain tissue is removed for study. However, any brain surgery carries risk of damage to the brain. Also, the tissue removed may not have been taken from the infected area. Thus, that tissue may not be the infected tissue. If this is the case, the biopsy may not help confirm or rule out the diagnosis. Finally, the risk of spreading infection with surgical tools is high. Thus, the surgery team must destroy the tools after surgery. An sCJD diagnosis also can be made from an autopsy of the whole brain. Autopsy is a study of the body performed after the person with the disease has died. Autopsy in sCJD is the only way to confirm the diagnosis with 100 percent accuracy. It also is useful for research.

Other tests commonly used for CJD diagnosis include:

- A blood test, to rule out other forms of dementia that may be treated
- A brain CT scan, to see if the person's symptoms are related to a stroke or brain tumor
- A brain MRI or EEG scan, to tell if an abnormality specific to CJD is present
- A spinal fluid test, to see if proteins that may cause dementia or CJD are present

#### WHAT IS THE 14-3-3 PROTEIN TEST? DOES IT HELP WITH DIAGNOSING CJD?

The 14-3-3 protein test is a test of the spinal fluid. The test looks for the presence of the 14-3-3 protein. This protein can be released into the spinal fluid when brain cells die. For this test, the doctor performs a lumbar puncture, also known as a spinal tap. This involves inserting a needle into an area below the spinal cord in the low back. The needle is used to obtain a sample of spinal fluid from that area. The sample is then tested for the presence of the 14-3-3 protein. The sample also may be tested to rule out other diseases.

In sCJD diagnosis, the 14-3-3 protein test may help support the diagnosis. There is moderate evidence that the test may support other tests for diagnosis in these situations:

- When a person shows signs of quickly progressing dementia
- When the dementia seems likely to be caused by sCJD

However, the 14-3-3 test has certain limitations. Taken alone, the test cannot prove an sCJD diagnosis. Moreover, the test results are not always accurate. Thus, the test cannot confirm that the disease is present in a given situation. Also, a negative test result cannot rule out the presence of the disease.

The 14-3-3 protein test may help only in certain situations. Only doctors experienced in diagnosing dementia can determine when the test is needed. In deciding if the test should be used, doctors consider a number of factors. These include:

- The fact that sCJD is rare
- · Information about the person obtained from the person's medical history or from a clinical exam
- The results of other tests already performed
- · How certain the doctor is about the cause or form of dementia involved

Likewise, only doctors should interpret test results. When analyzing the results, the doctor will take into account the test's limitations. In addition, the doctor may interpret the results differently depending on how strongly he or she suspects sCJD is present. This is because a positive result can occur even when the person does not have sCJD. In fact, such "false positives" are common in many disorders where there is a rapid loss of nerve cells. These disorders include:

- Acute stroke (sudden brain attack)
- Encephalitis (inflammation in the brain)
- Other disorders that involve dementia

A diagnosis of sCJD is serious. The disease progresses very quickly and eventually leads to death. Usually, death occurs within one year from symptom onset. If sCJD is diagnosed, it is important to discuss the diagnosis with a doctor experienced in diagnosing and managing the disease. In some cases, it can be helpful to find out if sCJD is the cause of dementia. Having this information may help to focus the person's care at a critical point in the disease.

This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

\*After the experts review all of the published research studies, they describe the strength of the evidence supporting each recommendation:

Strong evidence = more than one high-quality scientific study

*Moderate* evidence = at least one high-quality scientific study or two or more studies of a lesser quality *Weak* evidence = the studies, while supportive, are weak in design or strength of the findings

*Weak* evidence = the studies, while supportive, are weak in design or strength of the findings

Not enough evidence = either different studies have come to conflicting results or there are no studies of reasonable quality

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