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# REVIEW ON: CREUTZFELDT-JAKOB DISEASE

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## ABSTRACT

CJD is characterized by rapidly progressive dementia. Initially, individuals experience problems with muscular coordination; personality changes, including impaired memory, judgment, and thinking; and impaired vision. People with the disease also may experience insomnia, depression, or unusual sensations. CJD does not cause a fever or other flu-like symptoms. As the illness progresses, mental impairment becomes severe. Individuals often develop involuntary muscle jerks called myoclonus, and they may go blind. They eventually lose the ability to move and speak and enter a coma. Pneumonia and other infections often occur in these individuals and can lead to death, this review article describes introduction, signs and symptoms, diagnosis, causes, transmission, treatment of CJD.

## INTRODUCTION

What is Creutzfeldt-Jakob Disease, Creutzfeldt-Jakob disease (CJD) is a rare, degenerative, invariably fatal brain disorder. It affects about one person in every one million people per year worldwide; in the United States there are about 200 cases per year. CJD usually appears in later life and runs a rapid course. Typically, onset of symptoms occurs about age 60, and about 90 percent of individuals die within 1 year. In the early stages of disease, people may have failing memory, behavioral changes, lack of coordination and visual disturbances. As the illness progresses, mental deterioration becomes pronounced and involuntary movements, blindness, weakness of extremities, and coma may occur[1].

**There are three major categories of CJD:**

1. In sporadic CJD, the disease appears even though the person has no known risk factors for the disease. This is by far the most common type of CJD and accounts for at least 85 percent of cases.

2. In hereditary CJD, the person has a family history of the disease and/or tests positive for a genetic mutation associated with CJD. About 5 to 10 percent of cases of CJD in the United States are hereditary.

3. In acquired CJD, the disease is transmitted by exposure to brain or nervous system tissue, usually through certain medical procedures. There is no evidence that CJD is contagious through casual contact with a CJD patient. Since CJD was first described in 1920, fewer than 1 percent of cases have been acquired CJD.

CJD belongs to a family of human and animal diseases known as the transmissible spongiform encephalopathies (TSEs). Spongiform refers to the characteristic appearance of infected brains, which become filled with holes until they resemble sponges under a microscope. CJD is the most common of the known human TSEs. Other human TSEs include kuru, fatal familial insomnia (FFI), and Gerstmann-Straussler-Scheinker disease (GSS). Kuru was identified in people of an isolated tribe in Papua New Guinea and has now almost disappeared. FFI and GSS are extremely rare hereditary diseases, found in just a few families around the world. Other TSEs are found in specific kinds of animals[3]. These include bovine spongiform encephalopathy (BSE), which is found in cows and is often referred to as “mad cow” disease; scrapie, which affects sheep and goats; mink encephalopathy; and feline encephalopathy. Similar diseases have occurred in elk, deer, and exotic zoo animals.

**Symptoms of the CJ Disease:**

CJD is characterized by rapidly progressive dementia. Initially, individuals experience problems with muscular coordination; personality changes, including impaired memory, judgment, and thinking; and impaired vision. People with the disease also may experience insomnia, depression, or unusual sensations. CJD does not cause a fever or other flu-like symptoms. As the illness progresses, mental impairment becomes severe. Individuals often develop involuntary muscle jerks called myoclonus, and they may go blind. They eventually lose the ability to move and speak and enter a coma. Pneumonia and other infections often occur in these individuals and can lead to death.

**1. Dementia-** is a term that describes a collection of symptoms that include decreased intellectual functioning that interferes with normal life functions and is usually used to describe people who have two or more major life functions impaired or lost such as memory, language, perception, judgment or reasoning; they may lose emotional and behavioral control, develop personality changes and have problem solving abilities reduced or lost[2].

**2.Alzheimer's disease (AD):** is the most common cause of dementia in people over age 65 with cause possibly related to amyloid plaques and neurofibrillary tangles; almost all brain functions, including memory, movement, language, judgment, behavior, and abstract thinking, are eventually affected.

**3.Vascular dementia:** is the second most common cause of dementia caused by brain damage from cerebrovascular or cardiovascular problems (strokes) or other problems that inhibit vascular function; symptoms similar to AD but personality and emotions effected only late in the disease.

**4. Lewy body dementia:** is common and progressive where cells in the brain's cortex die and other contain abnormal structures (Lewy bodies); symptoms overlap with Alzheimer's disease but also include hallucinations, shuffling gait, and flexed posture with symptoms that may vary daily.

**5. Frontotemporal dementia:** is dementia linked to degeneration of nerve cells in the frontal and temporal brain lobes and some evidence for a genetic factor (many have a family history of the disease); symptoms in patients (usually ages 40 – 65) have judgment and social behavior problems such as stealing, neglecting responsibilities, increased appetite, compulsive behavior and eventual motor skill problems and memory loss[2].

**6. HIV-associated dementia:** is due to infection of the brain with HIV virus; symptoms include impaired memory, apathy, social withdrawal, and concentration problems.

**7.Huntington's disease:** is a heredity disorder caused by a faulty gene and children of a person with the disorder have a 50% chance of getting the disease; symptoms begin in 30-40 year old people with personality changes such as anxiety, depression and progress to show psychotic behavior severe dementia and chorea - involuntary jerky, arrhythmic movements of the body.

**8.Dementia pugilistica:** is also termed Boxer's syndrome, is due to traumatic injury (often repeatedly) to the brain; symptoms commonly are dementia and parkinsonism (tremors, gait abnormalities) and other changes depending where brain injury has happened.

**9.Corticobasal degeneration:** is a progressive nerve cell loss in multiple areas of the brain; symptoms begin at about age 60 on one side of the body and include poor coordination and rigidity with associated visual-spatial problems that can progress to memory loss, hesitant speech and dysphagia (difficulty swallowing).

**10. Depressive disorder:**

Depressive disorders have been with mankind since the beginning of recorded history. In the Bible, King David, as well as Job, suffered from this affliction. Hippocrates described the basic medical physiology theory of that time. Depression, also referred to as clinical depression, has been portrayed in literature and the arts for hundreds of years, but what do we mean today when we refer to a depressive disorder? In the 19th century, depression was seen as an inherited weakness of temperament. In the first half of the 20th century, Freud linked the development of depression to guilt and conflict[4,5]. John Cheever, author of depressive disorder, wrote of conflict and experiences with his parents as influencing his development of depression.

In the 1950s and '60s, depression was divided into two types, endogenous and neurotic. Endogenous means that the depression comes from within the body, perhaps of genetic origin, or comes out of nowhere. Neurotic or reactive depression has a clear environmental precipitating factor, such as the death of a spouse, or other significant loss, such as the loss of a job. In the 1970s and '80s, the focus of attention shifted from the cause of depression to its effects on the afflicted people. That is to say, whatever the cause in a particular case, what are the symptoms and impaired functions that experts can agree make up a depressive disorder? Although there is some argument today (as in all branches of medicines), most experts agree on the following:

A depressive disorder is a syndrome (group of symptoms) that reflects a sad and/or irritable mood exceeding normal sadness or grief. More specifically, the sadness of depression is characterized by a greater intensity and duration and by more severe symptoms and functional disabilities than is normal.

Depressive signs and symptoms are characterized not only by negative thoughts, moods, and behaviors but also by specific changes in bodily functions (for example, crying spells, body aches, low energy or libido, as well as problems with eating, weight, or sleeping). The functional changes of clinical depression are often called neurovegetative signs. This means that the nervous system changes in the brain cause many physical symptoms that result in diminished participation and a decreased or increased activity level. Certain people with depressive disorder, especially bipolar depression (manic depression), seem to have an inherited vulnerability to this condition. Depressive disorders are a huge public-health problem, due to its affecting millions of people. About 10% of adults, up to 8% of teens and 2% of preteen children experience some kind of depressive disorder.

**11. Insomnia:** is defined as difficulty initiating or maintaining sleep, or both, despite adequate opportunity and time to sleep, leading to impaired daytime functioning. Insomnia may be due to poor quality or quantity of sleep. Insomnia is very common and occurs in 30% to 50% of the general population[7]. Approximately 10% of the population may suffer from chronic (long-standing) insomnia. Insomnia affects people of all ages including children, although it is more common in adults and its frequency increases with age. In general, women are affected more frequently than men.

Situational and stress factors leading to insomnia may include:jet lag, physical discomfort (hot, cold, lighting, noise, unfamiliar surroundings),working different shifts,stressful life situations (divorce or separation, death of a loved one, losing a job, preparing for an examination), illicit drug use, cigarette smoking,caffeine intake prior to going to bed,alcohol intoxication or ithdrawal, or certain medications. Most of these factors may be short-term and transient, and therefore insomnia may resolve when the underlying factor is removed or corrected. Sleep hygiene Sleep hygiene can play an important role in insomnia. Poor sleep hygiene includes physical factors such as: using the bedroom for things other than sleeping, eating or exercising prior to sleep, going to bed hungry, sleeping in a room with too much noise or lighting, or doing

work in bed. Medical and psychiatric conditions Medical and psychiatric conditions may also contribute to insomnia. Some of these common medical conditions may include: breathing problems from chronic heart or lung disease (asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure, obstructive sleep apnea), obesity,

**Diagnosis of CJD:**

There is currently no single diagnostic test for CJD. When a doctor suspects CJD, the first concern is to rule out treatable forms of dementia such as encephalitis (inflammation of the brain) or chronic meningitis. A neurological examination will be performed and the doctor may seek consultation with other physicians. Standard diagnostic tests will include a spinal tap to rule out more common causes of dementia and an electroencephalogram (EEG) to record the brain's electrical pattern, which can be particularly valuable because it shows a specific type of abnormality in CJD. Computerized tomography of the brain can help rule out the possibility that the symptoms result from other problems such as stroke or a brain tumor[6]. Magnetic resonance imaging (MRI) brain scans also can reveal characteristic patterns of brain degeneration that can help diagnose CJD. The only way to confirm a diagnosis of CJD is by brain biopsy or autopsy. In a brain biopsy, a neurosurgeon removes a small piece of tissue from the patient's brain so that it can be examined by a neuropathologist. This procedure may be dangerous for the individual, and the operation does not always obtain tissue from the affected part of the brain. Because a correct diagnosis of CJD does not help the person, a brain biopsy is discouraged unless it is needed to rule out a treatable disorder. In an autopsy, the whole brain is examined after death. Both brain biopsy and autopsy pose a small, but definite, risk that the surgeon or others who handle the brain tissue may become accidentally infected by self-inoculation. Special surgical and disinfection procedures can minimize this risk. A fact sheet with guidance on these procedures is available from the NINDS and the World Health Organization.

Scientists are working to develop laboratory tests for CJD. One such test, developed at NINDS, is performed on a person's cerebrospinal fluid and detects a protein marker that indicates neuronal degeneration. This can help diagnose CJD in people who already show the clinical symptoms of the disease. This test is much easier and safer than a brain biopsy. The false positive rate is about 5 to 10 percent. Scientists are working to develop this test for use in commercial laboratories. They are also working to develop other tests for this disorder.

**Transmission of CJD:**

The defective protein can be transmitted by contaminated harvested human brain products, Immunoglobulins (IVIG), corneal grafts, dural grafts or electrode implants (acquired or iatrogenic form: iCJD); it can be inherited (hereditary or familial form: fCJD); or it may appear for the first time in the patient (sporadic form: sCJD). In the hereditary form, a mutation occurs in the gene for PrP, PRNP. Ten to 15 percent of CJD cases are inherited. (CDC)[8].

The disease has also been shown to result from use of Human Growth Hormone obtained from the pituitary glands of persons who died from Creutzfeldt–Jakob Disease, though the known incidence of this cause is (as of April 2004) quite small. The risk of infection via cadaveric HGH in the US ceased when the medication was withdrawn in 1985.

It is thought [citation needed] that humans can contract the disease by consuming material from animals infected with the bovine form of the disease. The only suspected cases to arise thus far have been CJD, although there are fears—based on animal studies—that consuming beef or beef products containing prion particles can also cause the development of classic CJD. When BSE material infects humans, the resulting disease is known as (new) variant CJD (nvCJD).

Cannibalism has also been implicated as a transmission mechanism for abnormal prions, causing the disease known as kuru, once found primarily among women and children of the Fore people in Papua New Guinea. While the men of the tribe ate the body of the deceased and rarely contracted the disease, the women and children, who ate the less desirable body parts, including the brain, were 8 times more likely than men to contract kuru from infected tissue.

Prions, the infectious agent of CJD, may not be inactivated by means of routine surgical instrument sterilization procedures. The World Health Organization and the US Centers for Disease Control and Prevention recommend that instrumentation used in such cases be immediately destroyed after use; short of destruction, it is recommended that heat and chemical decontamination be used in combination to process instruments that come in contact with high-infectivity tissues. No cases of iatrogenic transmission of CJD have been reported subsequent to the adoption of current sterilization procedures[9], or since 1976. Copper–hydrogen peroxide has been suggested as an alternative to the current recommendation of sodium hydroxide or sodium hypochlorite. Thermal depolymerization also destroys prions in infected organic and inorganic matter, since the process chemically attacks protein at the molecular level. CJD cannot be

transmitted through the air or through touching or most other forms of casual contact. Spouses and other household members of sporadic CJD patients have no higher risk of contracting the disease than the general population. However, exposure to brain tissue from infected individuals should be avoided to prevent transmission of the disease through these materials.

In some cases, CJD has spread to other people from grafts of dura mater (a tissue that covers the brain), transplanted corneas, implantation of inadequately sterilized electrodes in the brain, and injections of contaminated pituitary growth hormone derived from human pituitary glands taken from cadavers. Doctors call these cases that are linked to medical procedures iatrogenic cases. Since 1985, all human growth hormone used in the United States has been synthesized by recombinant DNA procedures, which eliminates the risk of transmitting CJD by this route[10].

The appearance of the new variant of CJD (nv-CJD or v-CJD) in several younger than average people in Great Britain and France has led to concern that BSE may be transmitted to humans through consumption of contaminated beef. Although laboratory tests have shown a strong similarity between prions causing BSE and v-CJD, there is no direct proof to support this theory.

Many people are concerned that it may be possible to transmit CJD through blood and related blood products such as plasma. Some animal studies suggest that contaminated blood and related products may transmit the disease, although this has never been shown in humans. If there are infectious agents in these fluids, they are probably in very low concentrations. Scientists do not know how many abnormal prions a person must receive before he or she develops CJD, so they do not know whether these fluids are potentially infectious or not. They do know that, even though millions of people receive blood transfusions each year, there are no reported cases of someone contracting CJD from a transfusion[11]. Even among people with hemophilia, who sometimes receive blood plasma concentrated from thousands of donors, there are no reported cases of CJD. While there is no evidence that blood from people with sporadic CJD is infectious, studies have found that infectious prions from BSE and vCJD may accumulate in the lymph nodes (which produce white blood cells), the spleen, and the tonsils. These findings suggest that blood transfusions from people with vCJD might transmit the disease. The possibility that blood from people with vCJD may be infectious has led to a policy preventing people in the United States from donating blood if they have resided for more than 3 months in a country or countries where BSE is common.`

**Treatment of CJD:**

As of 2011 no generally accepted treatment for CJD exists; the disease is invariably fatal and research continues. An experimental treatment was given to a Northern Irish teenager, Jonathan Simms, beginning in January 2003;The medication, called pentosanpolysulphate (PPS) and used to treat interstitial cystitis, is infused into the patient's lateral ventricle within the brain. PPS does not seem to stop the disease from progressing, and both brain function and tissue continue to be lost. However, the treatment is alleged to slow the progression of the otherwise untreatable disease, and may have contributed to the longer than expected survival of the seven patients who were studied The CJD Therapy Advisory Group to the UK Health Departments advises that data are not sufficient to support claims that pentosanpolysulphate is an effective treatment and suggests that further research in animal models is appropriate ,A 2007 review of the treatment of 26 patients with PPS finds no proof of efficacy because of the lack of accepted objective criteria[12,13].

Scientists have investigated using RNA interference to slow the progression of scrapie in mice. The RNA blocks production of the protein that the CJD process transforms into prions. This research is unlikely to lead to a human therapy for many years,

Both amphotericin B and doxorubicin have been investigated as potentially effective against CJD, but as yet there is no strong evidence that either drug is effective in stopping the disease. Further study has been taken with other medical drugs, but none are effective. However, drugs to reduce suffering do exist, and include Valproate, an anticonvulsant, and Clonazepam, to reduce muscle jerks.Dr. Michael Geschwind, Dr. Bruce Miller and Dr. Stanley Prusiner from University of California, San Francisco are currently running a treatment trial for sporadic CJD using quinacrine, a medicine originally created for malaria[14,15]. Pilot studies showed quinacrine permanently cleared abnormal prion proteins from cell cultures, but results have not yet been published on the clinical study.

**CONCLUSION**

Many researchers are studying CJD. They are examining whether the transmissible agent is, in fact, a prion or a product of the infection, and are trying to discover factors that influence prion infectivity and how the disorder damages the brain. Using rodent models of the disease and brain tissue from autopsies, they are also trying to identify factors that influence susceptibility to the

disease and that govern when in life the disease appears. They hope to use this knowledge to develop improved tests for CJD and to learn what changes ultimately kill the neurons so that effective treatments can be developed.

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