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CJD

Understanding Creutzfeldt-Jakob disease

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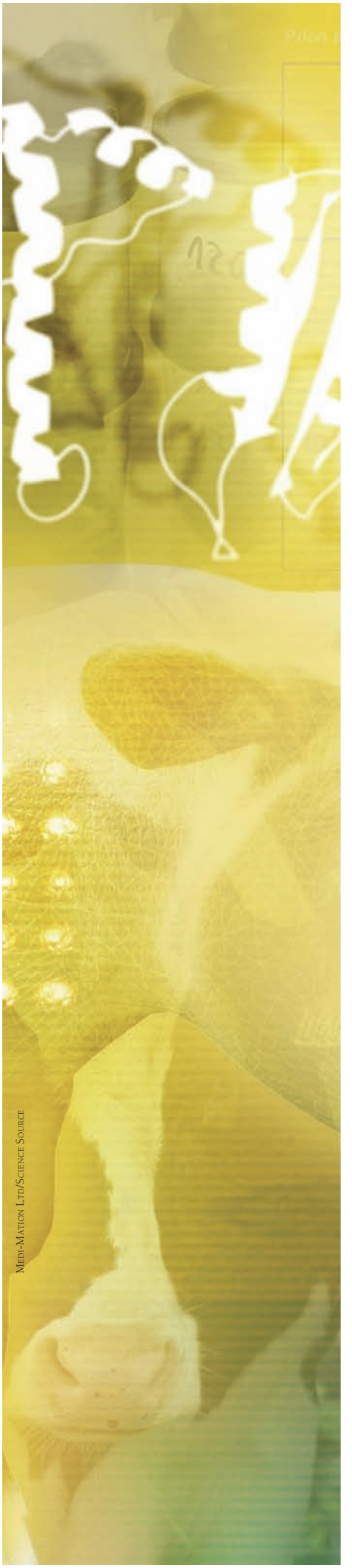
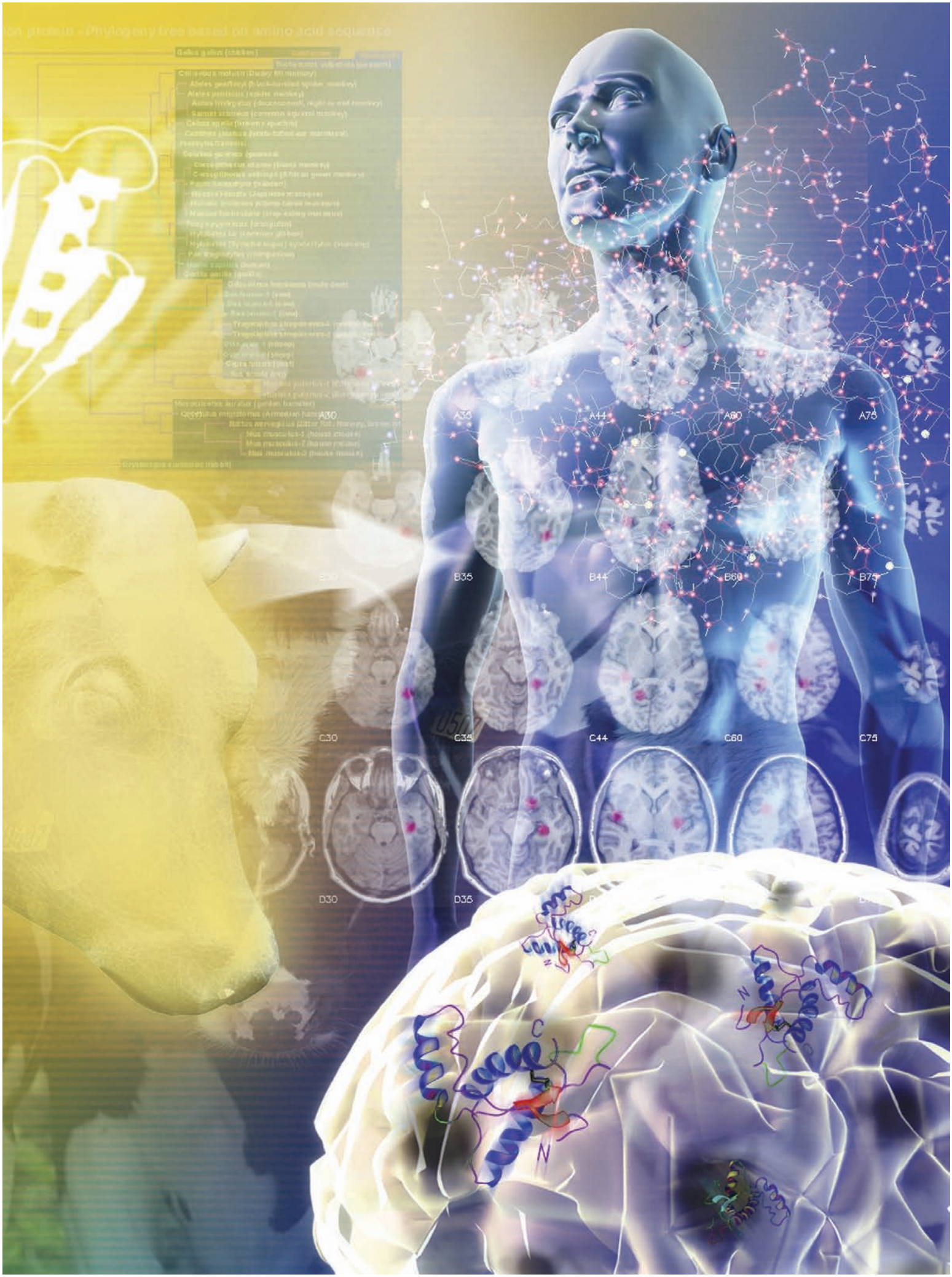
RARE, TRANSMISSIBLE, and rapidly progressive, Creutzfeldt-Jakob disease (CJD) is an ultimately fatal central nervous system infection caused by accumulation of abnormally shaped prion proteins in neurons (see *Understanding prion proteins*).[1] Although categorized as an infection, CJD doesn't lead to the immune system or inflammatory response typical of most infectious diseases. This article discusses the pathophysiology and diagnosis of this terminal illness and nursing care for patients with suspected or confirmed CJD.

Spongiform degeneration

CJD is an invariably fatal neurodegenerative disease without known treatment. It belongs to a group of transmissible brain disorders resulting from a structural abnormality of normal cellular proteins called prion proteins (PrP). These abnormal prion proteins (PrP^{SC}) are resistant to degradation and become widespread through the brain. They form a toxic aggregate causing spongiform degeneration of brain tissue, loss of neurons, and gliosis or scar formation in brain tissue. Spongiform refers to the sponge-like appearance of infected brain tissue when viewed under a microscope.[1-4]

CJD is the most common of the known human prion diseases, also called transmissible spongiform encephalopathies.[3] Prion diseases found





in animals include bovine spongiform encephalopathy (BSE), also called "mad cow disease," scrapie in sheep, feline encephalopathy, and chronic wasting disease found in mink and elk.[5]

The National Institute of Neurological Disorders and Stroke (NINDS), a division of the National Institutes of Health, recognizes three major categories of CJD:[3]

- Sporadic CJD (sCJD), which occurs spontaneously in people with no known risk factors for the disease. The most common type, sCJD accounts for at least 85% of all cases in the United States and worldwide and affects males and females equally. It's characterized by rapidly progressive clinical deterioration leading to death within months.[1,6]
- Familial or hereditary CJD (hCJD). Patients with this type have a family history of CJD or test positive for a genetic mutation associated with CJD. From 5% to 10% of CJD cases are diagnosed hCJD in the United States.[3]
- Acquired (iatrogenic) CJD (aCJD). Transmitted by exposure to infectious brain or nervous system tissue or contaminated neurosurgical instruments, aCJD is usually associated with surgical or medical procedures. Since CJD was first described in 1920, aCJD has accounted for less than 1% of all cases of CJD.[3]

A variant form of CJD (vCJD) is a recognized type of CJD but not a major category. It's thought to be transmitted by ingesting beef infected with BSE.[3,7]

Because sCJD is the most common type by far, it's the focus of this article.

Myoclonus and other signs and symptoms

sCJD usually appears later in life; the mean age for symptom onset is between 55 and 75. Following onset of symptoms, the median duration of survival is approximately 4.5 months. Most (about 90%) of affected patients survive less than 1 year.[2,3]

Understanding prion proteins[2, 20-23]

Prion proteins are glycoproteins that occur in both a normal and an infectious form. The normal form is present in nervous system and other cells. The function of prions is not entirely known or understood; however, they may play a role in long-term memory.

Both normal and infectious forms of prion proteins share the same sequence of amino acids, but the infectious form of the protein has a misfolded shape different than the normal prion protein. The pathogenesis of CJD is believed to be due to a conformational change in normal prion proteins (PrP) to a pathologic misfolded form referred to as scrapie prion proteins (PrP^{sc}). All prion proteins are self-replicating and protease-resistant, making them resistant to degradation. All forms of CJD are associated with the pathologic PrP^{sc}.

As PrP^{sc} get into brain cells, they're believed to cause surrounding normal PrP to misfold and become both infectious and nonfunctional. This process is self-perpetuating. The dead brain cells release more misfolded PrP^{sc}, which infect surrounding normal brain cells, destroying them too. The PrP^{sc} aggregate and clump together, leading to neuronal loss and spongiform brain tissue. The damage caused by PrP^{sc} leads to neuromuscular deterioration and other signs and symptoms associated with CJD.

Growing evidence suggests that prion-like mechanisms may also have a role in other more common neurodegenerative disorders such as Alzheimer disease, amyotrophic lateral sclerosis, and Parkinson disease. In contrast to Alzheimer disease and other forms of dementia, most cases of CJD are associated with a more rapid deterioration of cognitive abilities.

Early signs and symptoms of sCJD include personality and behavioral changes, failing memory, unstable gait, myoclonus, and vision disturbances. Myoclonus, a characteristic feature of sCJD, presents as irregular short-duration muscular jerk-like episodes. Damage to the motor cortex or motor pathways in the brain affects muscles with the greatest cortical representation, such as the limbs, digits and face, but myoclonus can affect any muscle or muscle group.[1,4]

Diagnosis may be delayed because signs and symptoms of sCJD mimic many nonprion neurologic conditions including stroke, dementia such as Alzheimer disease, or multiple sclerosis.[2,8] Differentiating CJD from nonprion diseases is important because, unlike CJD, many nonprion, rapidly progressive dementias respond to treatment or in some cases are even curable.[2,8-10]

Common findings of suspected sCJD on neurologic examination include features such as rapidly progressive dementia, myoclonic muscle jerks, visual disturbances, and cerebellar ataxia including loss of coordination, gait instability, and uncoordinated eye movements. These signs are nonspecific, may not affect all individuals with sCJD, and can be caused by various diseases besides sCJD. Because early spongiform changes and neuronal loss can be subclinical, initial presentation may occur in the late or advanced stages of the disease process.[11]

Diagnosis

Because CJD has no typical presentation and may be mistaken for other disorders, diagnosis is challenging and may be delayed or missed. Other neurologic diseases and disorders that can cause similar signs and symptoms must be ruled out, such as subarachnoid hemorrhage, encephalitis, meningitis, acute ischemic stroke,

Diagnostic criteria for suspected CJD[24,25]

Possible diagnosis	Probable diagnosis	Definite diagnosis
Progressive dementia and at least two of the following four clinical features: • myoclonus • visual or cerebellar signs • pyramidal or extrapyramidal signs such as cogwheel rigidity • akinetic mutism (inability to speak or move, minimal responsiveness, eyes may be open)	Rapidly progressive dementia and at least two of the following four clinical features: • myoclonus • visual or cerebellar signs • pyramidal (weakness) or extrapyramidal (movement) signs • akinetic mutism	Brain tissue sample examined by standard neuropathologic techniques and/or immunocytochemical methods and/or Western blot to confirm presence of protease-resistant PrP and/or scrapie-associated fibrils
AND the absence of a positive result for any of the three lab tests that would classify a case as "probable."	AND a positive result on at least one of the following lab tests: • EEG (periodic sharp wave complexes) during an illness of any duration • positive 14-3-3 CSF assay with a disease duration of less than 2 years • MRI high signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging or fluid attenuated inversion recovery	
AND duration of illness less than 2 years	AND no alternative diagnosis indicated by routine investigations.	
AND no alternative diagnosis indicated by routine investigations.		

multi-infarct dementia, brain neoplasms, paraneoplastic neurologic disorders and, as previously discussed, nonprion forms of dementia such as Alzheimer disease.[2,4]

A brain tissue biopsy with histologic analysis of the sample is currently the only accepted definitive, gold standard diagnostic test for CJD. However, performing a timely brain tissue biopsy isn't always possible. In addition, because a positive brain tissue biopsy result wouldn't change the disease course or care plan, the risks may outweigh the benefits. Typically, diagnosis of CJD depends on clinical suspicion based on signs and symptoms at presentation and a thorough assessment of medical, surgical, dietary, and family history. (See *Diagnostic criteria for suspected CJD*.)

Rapid and accurate diagnosis of CJD, regardless of type or variant, is important to prevent the iatrogenic spread of the disease via certain tissue transplants, such as dura mater or corneal transplants, or through use of contaminated or inadequately sterilized neurosurgical instruments.

Diagnostic tests include magnetic resonance imaging (MRI), electroencephalogram (EEG), and cerebrospinal fluid (CSF) analysis.

- MRI has had the greatest impact on accurately diagnosing CJD without a brain tissue biopsy. Advanced MRI techniques such as diffusion weighted imaging and fluid level attenuated inversion recovery images will reveal characteristic changes consistent with tissue damage caused by CJD. These changes can be seen in specific regions of the brain, including the basal ganglia, thalamus, and cortex.[2,4]
- An EEG may show abnormal periodic sharp wave complexes.[4]
- A lumbar puncture is performed to obtain a CSF sample to test for a protein called 14-3-3. The 14-3-3 CSF assay was developed by NINDS. However, some reports indicate that a positive 14-3-3 result can reflect acute neuronal damage not necessarily caused by infectious prion proteins.[10] Consequently, a positive 14-3-3 CSF result alone isn't considered sufficient evidence to diagnose CJD. Some researchers recommend testing CSF for tau protein, which has been shown to be more reliable as a marker for CJD than the 14-3-3 protein.[2] All of these tests are typically performed after an individual displays signs and symptoms suspicious for CJD.[2,4]

Beware of these modes of transmission

Regardless of type or variant, CJD isn't transmitted through air, touch, or other forms of casual contact.

However, it can be transmitted via exposure to central nervous system tissue, the food chain, or improperly sterilized neurosurgical instruments.[12,13]

Human tissues considered to be highly infective include brain, spinal cord, pituitary gland, and eye tissues. CJD has been transmitted in dura mater tissue grafts and transplanted corneas. CSF is also considered infective, but urine, feces, sweat, mucus, and blood are not.[14,15]

Because PrP^{sc}, the abnormal prion proteins that cause CJD, are resistant to heat, radiation, and disinfectants, inadequately sterilized neurosurgical instruments and reusable deep brain electrodes are recognized as potential sources for transmission. Acquired cases of CJD have decreased dramatically with improved sterilization procedures, disposal of instruments, and use of single-use neurosurgical instruments in patients infected with PrP^{sc}. However, healthcare professionals must be aware that normal sterilization and disinfectant procedures don't destroy PrP^{sc}. The World Health Organization has issued detailed infection control guidelines, including recommendations for decontamination of work surfaces and surgical instruments, that are available for downloading.[12,14]

In 1985, when three people previously treated with human pituitary growth hormone (hGH) died of CJD, the United States Department of Health and Human Services immediately halted distribution of hGH and began a national study to learn more about how growth hormone therapy may have caused this problem. Beginning in 1997, a highly selective step was added to the growth hormone purification protocol that markedly reduces prion contamination and infectivity. Since then, hGH used for treatment has posed no threat of infection.[3,16]

Although no evidence indicates that blood donated from people with sCJD is infectious, research has shown that infectious prions from BSE and vCJD may accumulate in the lymph nodes, the spleen, and the tonsils. Because this raises the possibility that vCJD could be transmitted via blood transfusions, policy in the United States bars blood donation from people who've resided for more than 3 months since 1980 in a country where BSE is common, as well as from people who are blood relatives of someone with CJD.[3,15] However, Yang et al. report that the risk of acquiring transfusion-transmitted vCJD in the United States is both highly uncertain and likely very small.[17]

Infection control precautions for patients with known or suspected CJD[6,12-14,26]

Use standard precautions when caring for any patient with known or suspected CJD or any other prion disease and for those at high risk for development of a prion disease, such as patients with rapidly progressive dementia or who've received a dura mater transplant. Contact precautions aren't necessary for routine care but as always, wear gloves to handle blood and body fluids, and wear gowns and protective eyewear if exposure to blood or other potentially infectious material is possible. Follow your facility's infection control policy and procedure as well as these general guidelines.

- Because standard decontamination of tissue samples (for example, with formalin) may not inactivate CJD, all tissue samples must be handled using standard precautions. According to facility policy, label tissue samples and specimens as a "biohazard" and as "suspected CJD" before sending them to the lab.
- No special precautions are required for disposal of body fluids, which may be disposed of via a sanitary sewer. Blood or blood-contaminated fluids should be managed according to state regulations for regulated medical waste.
- A private hospital room isn't required for infection control, and no special precautions need to be taken with eating utensils, linens, feeding tubes, or suction tubes. Laundry should be managed as required by the Occupational Safety and Health Administration (OSHA) rule on blood-borne pathogens.
- Patients with any known or suspected prion disease shouldn't serve as donors for organs, tissues, blood components, or hormones.
- Infection control professionals and other departments involved with infection control (such as surgical services, central processing, and pathology) should be notified when a patient with a known or suspected prion disease is scheduled to undergo any invasive procedure in which personnel or instruments may be exposed to potentially infectious tissues.
- When a patient dies, ensure that the morgue and funeral home are notified that the patient had CJD.

Follow standard precautions

Because CJD isn't transmitted via casual contact, the CDC doesn't recommend contact precautions for those caring for patients with any form of CJD. However, as with any patient, caregivers should observe standard precautions to prevent contact with blood and other body fluids, particularly CSF. If a patient with CJD has another infection that can be spread by contact, droplet, or airborne mechanisms, appropriate infection control precautions must be maintained throughout the course of the disease.[13,18] (See *Infection control precautions for patients with known or suspected CJD*.)

Nursing challenges

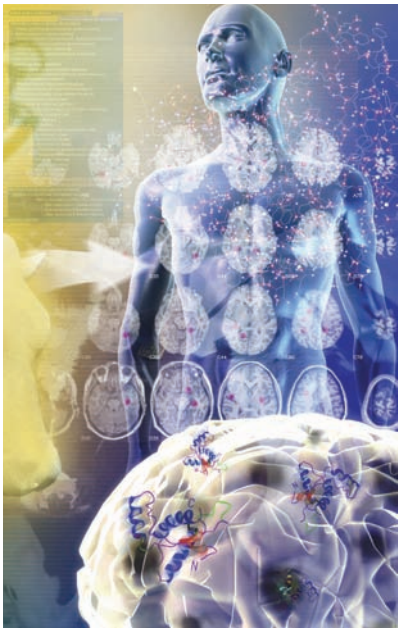
Nurses provide comprehensive care to patients with a suspected or confirmed CJD diagnosis and are often

present when the diagnosis of CJD is given to the patient and family. The complexity of CJD, with its neurologic clinical manifestations and rapid course presents myriad nursing care challenges.

Because CJD is progressive and usually rapidly terminal, patients and families struggle to understand and accept this devastating diagnosis. Nurses caring for patients and families are challenged to understand the nature of CJD, manage the patients' signs and symptoms, and create a therapeutic experience by integrating the psychological, emotional, spiritual, and social components of nursing care. Nurses must also educate patients and families about infection control strategies, such as practicing standard precautions in the hospital and at home.

In addition, nurses must be prepared to guide, educate, and support patients and families as they prepare for the patient's death. This can involve helping them with resources for updating legal documents such as advance care directives, referring them to support systems and resources, and even discussing issues surrounding funerals, autopsy, and burial. The plan of care for the patient and family affected by CJD, as with all patients, must be relevant, understandable, consistent with their beliefs, and culturally appropriate.[18,19]

Management of CJD is guided by symptom relief. As the patient's condition progresses, nurses should anticipate psychiatric signs and symptoms such as hallucinations, mood swings, and aggressive behavior, and initiate appropriate interventions.[12] Aggression, agitation, and restlessness can be treated with benzodiazepines or antipsychotics such as risperidone. Antidepressants might be prescribed for depression or anxiety symptoms. Clonazepam and sodium valproate may help treat myoclonus. Although CJD doesn't cause a fever or other flu-like symptoms, analgesics may be prescribed to help relieve pain if present.[3]



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As CJD progresses, the patient will become bedbound and require assistance with repositioning, feeding, and hygiene. Nursing care includes frequent repositioning to prevent discomfort and pressure ulcers. For patients who can't control bladder function, an indwelling urinary catheter may be indicated.

Early diagnosis and surveillance

All types of CJD are progressive, incurable, and transmissible, so the sooner the diagnosis can be established, the better. Early diagnosis helps control the spread of disease and may contribute to development of effective treatments. Because of variable clinical presentations associated with CJD and the lack of specific diagnostic procedures beyond brain tissue biopsy, the ante-mortem diagnosis of CJD is challenging and it's likely that many cases are undiagnosed.

The National Prion Disease Pathology Surveillance Center (NPDPSC), established by the CDC in collaboration with the American Association of Neuropathologists, makes prion disease testing available free of charge to healthcare providers. The NPDPSC can confirm or refute the CJD diagnosis and may also detect other unusual or new prion diseases. The NPDPSC also makes tissue samples collected at autopsy available to labs for research into prion diseases such as CJD.[20]

An important and useful resource for patients and families affected by CJD is the Creutzfeldt-Jakob Disease Foundation, a nonprofit organization dedicated to support the patients and families affected by CJD. It can be accessed online at http://cjdfoundation.org or via the CJD help line at 1-800-659-1991.[19] ■

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