Creutzfeldt-Jakob Disease

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Creutzfeldt-Jakob Disease (CJD) is a rare, fatal neurological disorder, which causes rapid, progressive dementia and associated neuromuscular disturbances. This form of prion disease affects approximately one in one million people per year worldwide.[10] Most cases occur in patients between 50 and 70 years of age. The duration of illness after patients become symptomatic is an average of six months. At the present time, no treatments exist for CJD; the disease always ends in death.

Creutzfeldt-Jakob Disease was first reported in medical literature in the 1920s when Drs Jakob and Creutzfeldt reported cases of a transmissible and fatal neurodegenerative disease. Recent outbreaks of Mad Cow Disease in Europe and a misunderstanding of this disease have heightened the public's fear of a CJD outbreak among humans.

Transmission

General etiology

Cases of CJD have been classified by etiology as inherited, iatrogenic, or sporadic. Genetic or inherited CJD accounts for only 5% to 10% of the total number of cases. Inherited forms of prion disease include CJD, fatal familial insomnia (FFI), and Gerstmann-Straussler-Scheinker syndrome (GSS).

Approximately 90% of CJD cases are sporadic. When CJD occurs as a sporadic disease, no recognizable pattern of transmission has been reported. Researchers have found that prions occur naturally in humans but in a slightly different shape (Figure 1). The pathogenic shape is folded (Figure 2) and researchers hypothesize that a mutation, followed by an infectious altering of normal prions, leads to the spontaneous form. Reasons for this mutation remain unclear.[11,13]

Of the three forms of CJD, iatrogenic CJD occurs in less than 1% of the cases.[2] There have been documented cases of iatrogenic transmission of CJD linked to pituitary extracts (including human growth hormone), dura mater, corneal transplants, and to instruments and devices that have penetrated the brain, such as stereotactic electrodes.[6]

New variant CJD

A new variant of the disease, vCJD or nvCJD, has been documented in the United Kingdom and several other European countries. New variant CJD is linked to eating beef from cattle infected with bovine spongiform encephalopathy (BSE), also called Mad Cow Disease. This form of the disease afflicts individuals between 16 and 48 years of age. Onset of symptoms is much quicker and duration can last up to 14 months. Pathology of vCJD (characterized by amyloid plaques) differs significantly from that of normal CJD, and patients tend to get a related form of tonsil disease, which may make it easier to diagnose.[12]

Diagnosis

CJD is one of a group of encephalopathies known as transmissible spongiform encephalopathies (TSEs), characterized by the sponge-like pathology of the brain.[12] The incubation period for CJD can vary from years to decades. Symptoms including depression, poor memory and, in latter stages, dementia and loss of physical functioning, may take decades to appear. The organism was originally labeled a "slow virus" because of the long incubation period. (Variant CJD is characterized by a more rapid onset of clinical symptoms.)

A definite diagnosis of CJD requires a histologic examination of the affected brain tissue.[8] Craniotomy and stereotactic brain biopsy can be utilized to obtain brain tissue. Ideal sampling includes thalamus, cerebellum, all cortical lobes, the basal ganglia, and brain stem, so definite diagnosis is usually not obtained until a postmortem autopsy.[2] Reported in most CJD patients has been the presence of 14-3-3 protein in the cerebrospinal fluid and/or atypical electroencephalogram (EEG) pattern, both of which are believed to be diagnostic.[1]

Causative agent

Prions, proteinaceous infectious particles, are believed to cause CJD. Prions are unlike all other known pathogens. They do not contain genetic material and have the unique ability to survive routine sterilization and disinfection processes. Several recent reports issued by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the Centers for Disease Control (CDC) have signaled a renewed awareness of preventative infection control measures. (See "Much Ado About Prions," page 13)

Infection control case study

Exempla Saint Joseph Hospital in Denver, Colorado, encountered exposure to CJD in 2000. Hospital officials have encouraged JCAHO to share the results of a root cause analysis with other health care organizations in order to prepare risk reduction strategies. A patient who did not present with CJD symptoms underwent brain biopsy to rule out vasculitis in November

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Much ado about prions

When Stanley Prusiner introduced the prion (pronounced "pree-on"), short for a proteinaceous infectious particle, in 1982, the idea was considered preposterous. (See History of Surgery, page 26) Prusiner's prion theory was controversial because the scientific community believed that infectious material had to contain genetic material such as DNA or RNA. The human body is built from proteins: How could one be infectious?[13,14]

Prusiner resolved to find the answer. He and his associates confirmed that the human body naturally produces the same protein responsible for CJD, called PrP, but that protein's structure is slightly different than that of an infectious protein, or prion.[13] Natural PrP was discovered on nerve cells, white blood cells, muscle cells and in other tissues throughout the body. This protein consists of three helix-shaped chains comprised of 208 amino acids and a tail of 27 amino acids extending from one end.[11]

In its infectious form, PrP changes from an alpha-helical (spiral) shape to a beta-sheet (folded or accordion) form. Upon contact with normal PrP, a prion creates a chain reaction that replicates itself by "folding" the alpha form into a beta configuration. Several theories attempt to explain how the beta-sheet prion converts normal PrP, but none of those theories have been proven.[14]

In the brain, the PrP converts from the alpha-helical form to the beta-sheet form inside neurons. The beta-sheet prions accumulate in the lysosomes, eventually killing the neuron (the action of which is still unknown). Death of the neurons creates sponge-like holes in the brain and releases the prions to infect neighboring neurons.[14]

Scientists have linked inherited forms of CJD to a DNA mutation on codon 102, and later discovered mutations in the genetic code for FFI and GSS. These DNA mutations create an inherited susceptibility to prion disease, but the disease won't develop unless the alpha form flips into the beta form.[13,14]

Although prions are an infectious agent, prion diseases are not contagious in the same way as viruses or bacteria. Human-to-human transmission is a consequence of tainted instruments during a medical procedure or tissue transplantation from an infected individual.[15]

Prion diseases exist in humans, but are more common in animals. Animal forms of prion disease include bovine spongiform encephalopathy (Mad Cow Disease), scrapie (sheep), transmissible mink encephalopathy, feline spongiform encephalopathy, and chronic wasting disease (mule deer and elk).[13]

The PrP protein sequence is key to understanding a species ability' to develop prion disease. If two species have a similar amino acid sequence in susceptible positions of their PrP, exposure is more likely to create the disease.[13] It is a well-known fact that bovine spongiform encephalopathy originated from adding ground-sheep parts to feed given to cows.[11,13] PrP proteins in cattle and sheep differ at seven positions, making the disease easily transferrable between species. Although human and cattle PrP differ at more than 30 positions, they are similar at specific vulnerable regions, making humans susceptible.[13,14]

Much about prions remains a mystery. Scientists continue their search for a better understanding of and a cure for prion diseases.

They hope this body of knowledge will also shed light on other neurological disorders, such as Alzheimer's and dementia.

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FIGURE 1

Normal PrP is found on nerve cells, white blood cells, muscle cells and other tissues throughout the human body.

2000. The patient died in December 2000 and following a postmortem brain biopsy, Creutzfeldt-Jakob disease was confirmed. In the meantime, six patients underwent brain biopsy procedures using the same sterilized instruments.[3]

Exempla Saint Joseph Hospital had a manual tracking system in place that identified patients that were operated on using those specific surgical instruments. The hospital informed the six patients about their possible exposure to CJD. Similar incidents have occurred at the Hotel-Dieu Hospital in Canada and at Tulane University Hospital in Louisiana.[3]

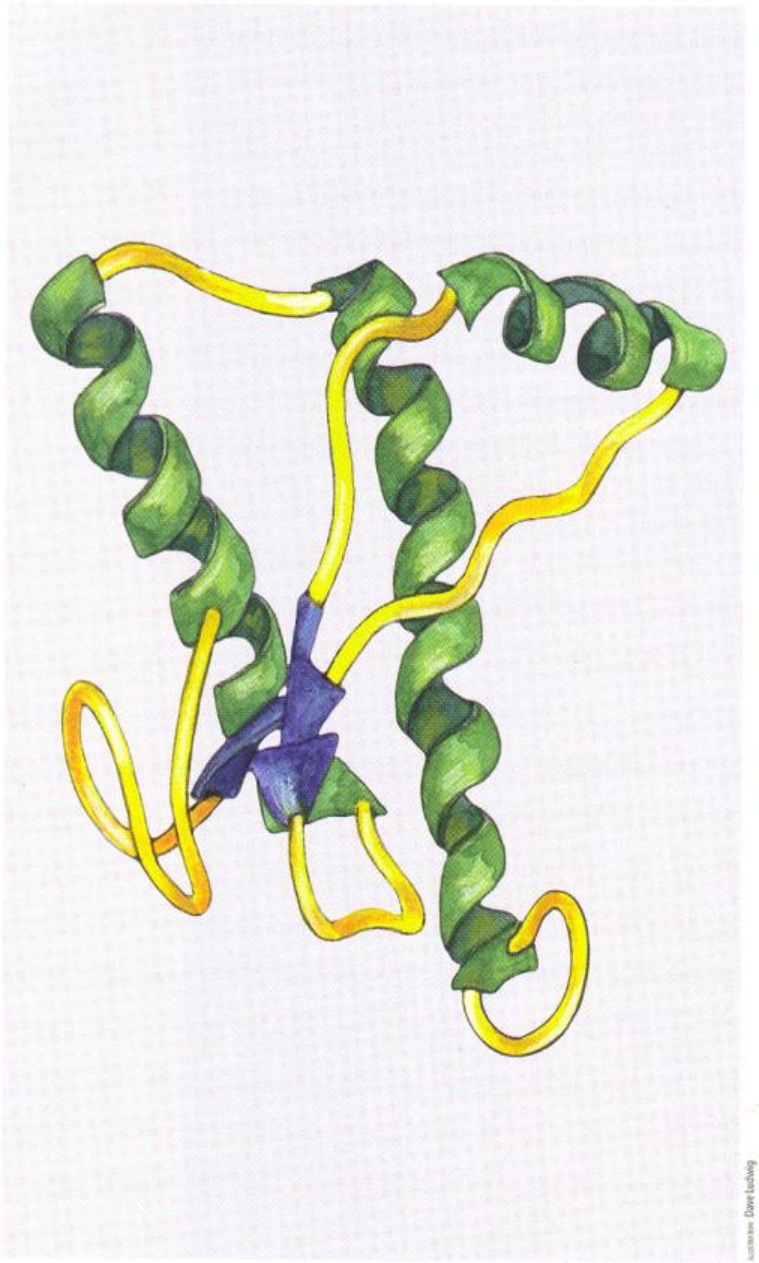

Illustration: Dave Ludwig

The risk of infection from contaminated surgical instruments is remote, but the lack of effective and reliable screening methods for patients with CJD has elevated the fear of an outbreak. Adding to the confusion of this disease's prognosis is the lack of well-defined protocols for addressing and resolving a potential CJD outbreak. The extremely low risk of CJD transmission during surgery ironically further complicates outbreak investigations.[5]

The hospital's root cause analysis involved sterilization and use of instruments, communication, competency of staff, and the interval between biopsy and pathology report. The hospital learned three important lessons[3]:

1. Instruments used during brain biopsy procedures should not be reused when the patient's diagnosis is uncertain at the time of the procedure.
2. CJD or prion disease patients do not always present with symptoms of CJD.
3. The time interval between the biopsy report and the pathology report should be closely monitored and reviewed to assure the shortest time from biopsy to results.

Other risk reduction strategies identified by Exempla Saint Joseph Hospital include[3]:

- Incinerate brain surgery instruments used on confirmed CJD patients.
- Quarantine neurosurgery instruments until physicians rule out CJD.
- Educate staff members, primary care physicians, and clinicians.
- Develop policies, procedures, and guidelines for suspected CJD cases in the operating room.

Recommendations

JCAHO recommends that organizations establish policies for 1) the disinfection or disposal of instruments used in neurosurgery in general and when CJD is suspected or confirmed and 2) the quarantine of such surgical instruments until an unclear diagnosis or biopsy is clarified. The World Health Organization's Infection Control

Guidelines for Transmissible Spongiform Encephalopathies also recommends the use of single-use surgical instruments and the destruction of reusable instruments that come in contact with highly infective tissues.[3]

Prions show considerable resistance to conventional chemical and physical sterilization methods such as ethylene oxide, boiling, dry heat, and autoclaving by conventional protocols.[9] Many recommendations have been offered about instrument reprocessing. Some literature suggests discarding all instruments no matter what organ system they were used on.

New guidelines

Recently, two highly respected experts in healthcare decontamination and sterilization science have challenged guidelines provided by the World Health Organization. William Rutala, PhD, and David Weber, MD, MPH, have challenged most of what has been previously published on processing instrumentation. Rutala and Weber suggest being proactive and not waiting until after the diagnosis to react.

Experts on CJD agree that not all tissue has the same level of risk of transmission. High-risk tissues include: eye tissue, dura mater, brain, and spinal cord. Significantly less infective tissues include: lymph nodes, lung, liver, kidney, spleen, and cerebral spinal fluid.[6]

Rutala and Weber suggest that the choice of sterilization methods for devices used on CJD patients depends on the type of device and the tissues to which it is exposed. The authors classify devices as: "critical," devices that enter sterile tissue or the vascular system (eg, surgical instruments and implants), "semicritical," devices that contact mucous membranes and broken skin (eg, endoscopes), and "noncritical," items that touch intact skin but not mucous membranes (eg, blood pressure cuffs).[7]

A critical or semicritical device that has contact with high-risk tissue from a high-risk patient must be processed in a manner to ensure the elimination of prions. Critical or semicritical devices that have contact with low-risk or no-risk tissue can be treated by means of conventional methods, because the devices have not resulted in the transmission of CJD.[9]

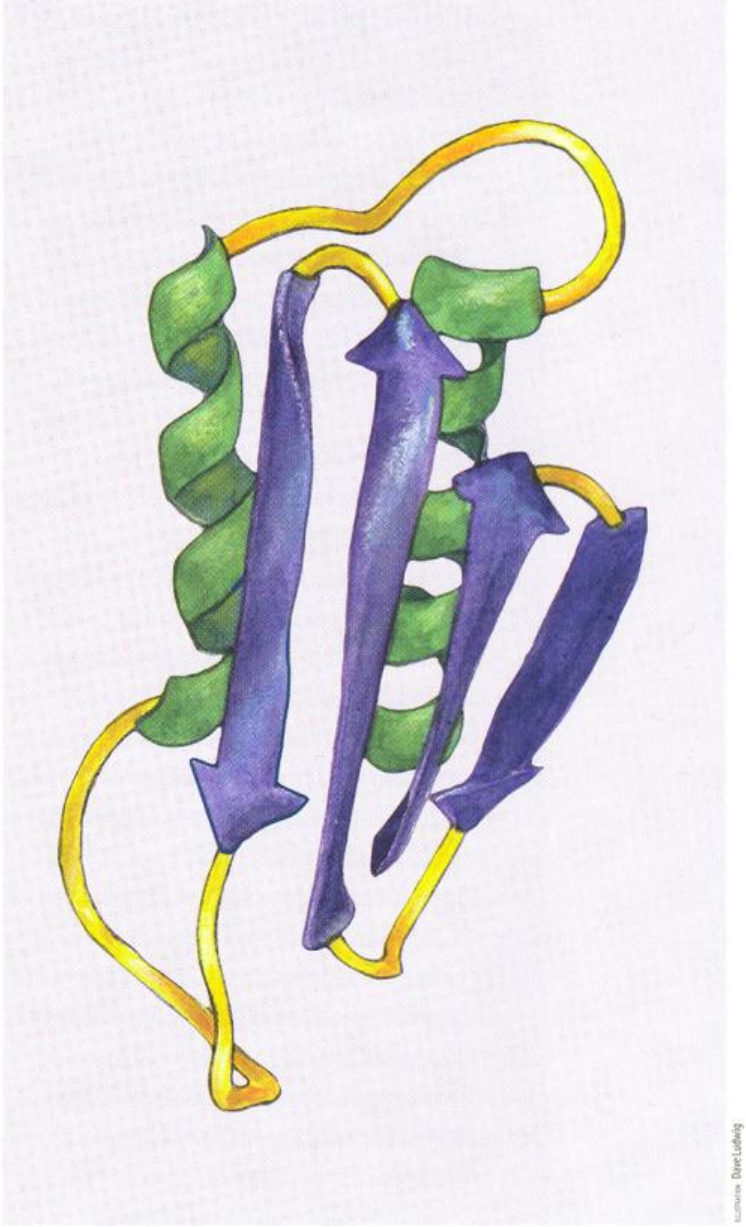

FIGURE 2

Prions, infectious PrP, are characterized by folded or accordion sections. Normal PrP is helical.

CDC guidelines

The Centers for Disease Control has worked on various guidelines relating to the processing of potentially CJD-contaminated instruments since 1985, and the CDC's Healthcare Infection Control Practices Advisory Committee (HICPAC) is working on guidelines now. Rutala and another colleague, Martin Favero, PhD, recently presented the following two CDC draft guidelines[7]:

1. High-Risk Patient, High-Risk Tissue, Critical or Semicritical Device, a Modified Processing Protocol is recommended[7]:

Sample guidelines for suspected CJD cases[4]

Preoperatively

- Notify all units potentially involved.
- Remove all extraneous equipment from the room (as much as possible) and move everything else as far from the operating table as possible.
- Cover all surfaces (including respiratory and anesthetic equipment) and OR table with impervious sheets.
- Cover electrical cords with sterile sleeves/plastic.

Intraoperatively

- Try to use disposable equipment and instruments whenever possible.
- Avoid using power instruments to prevent aerosolization of contaminates.
- Do not pass sharps from hand to hand. Always use a neutral zone to pass instruments.
- Attire: impervious gowns, hats, double gloves, masks, face shields, and knee-high impervious shoe covers.
- Clean spills of blood and body fluids with sodium hydroxide as they occur.
- Surgeon should change to new sterile gloves after the biopsy has been obtained.
- Tissue specimens are placed into a specimen container, placed into a biohazard specimen bag, and labeled "CJD precautions."
- The patient's head may be cleansed with 1 Molar sodium hydroxide at the completion of the case, per surgeon order.

Postoperatively

- Instrument handling: Place reusable instruments in an impervious container, red bag and label as "possible CJD."
- Body fluids/liquid waste: Should be collected, solidified, labeled and bagged as biohazardous and "possible CJD." Segregate waste from other red bag waste so that it can be incinerated.
- Other disposable supplies: All trash including surgical attire, drapes, Mayo covers, sponges, etc. should be placed in red bags and labeled as "possible CJD" and kept separate from other red bag trash, so that it can be incinerated. All disposable sharps should be placed in a sharps container and labeled as "possible CJD."
- Standard precautions should be used in the postoperative care of the patient's wound.

Environmental cleaning

- Decontaminate surfaces at the end of the procedure by continually wetting all exposed surfaces with 1 Molar sodium hydroxide for 60 minutes. Rinse thoroughly with water, then proceed with regular cleaning.
- Environmental surfaces contaminated with visible tissue should be decontaminated with 1:10 dilution of 5.25% sodium hypochlorite, followed by routine cleansing with hospital disinfectant.

- Steam autoclaving for previously cleaned instruments:
  134° C (272° F) for 18 minutes or
  121° C (250° F) for 1 hour
- For instruments that are difficult to clean:
  Soak 1 hour in 5,000 parts per million hypochlorite or 1 molar (M) sodium hydroxide,
  Then rinse, clean, and autoclave as above.

2. Conventional Disinfection and Sterilization Protocols are Suitable for the Following Situations[7]:

- High-risk patient/medium-to-low-risk tissue/critical or semicritical device
- Low-risk patient/high-risk tissue/critical or semicritical device
- High-risk patient/high-risk tissue/noncritical device
- Medium-, low-, or no-risk tissue/high-risk patient/critical or semicritical device

Conclusion

Many questions still remain about Creutzfeldt-Jakob disease and controversy surrounds sterilization and disinfection guidelines recently issued by professional organizations. Written protocols are essential, and each healthcare organization is urged to review their policies and procedures for processing instrumentation used

on possible CJD patients. Guidelines should be prepared to include the following departments: nursing, pharmacy, central processing, infection control, environmental services, laboratory, and surgical services. Policies should be developed to include instrument handling, storage, cleaning, and decontamination or disposal. All staff members and physicians should be aware of the recommended precautions and policies. Healthcare professionals should continue to seek the most current research materials and be prepared to update policies and procedures as new recommendations are developed.

About the author

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References

1. Centers for Disease Control. Questions and answers regarding Creutzfeldt-Jakob disease infection control practices. ***www.cdc.gov/ncidod/diseases/cjd/cjd_inf_ctrl_qa.htm***
2. Hansel P. Mad cow disease-the OR connection. *AORN Journal.* 1999;70(2):224-238.
3. Joint Commission on Accreditation of Healthcare Organizations. Sentinel Event Alert. Issue 20. June 2001. Oakbrook Terrace, IL: Exposure to Creutzfeldt-Jakob Disease. ***www.jcaho.org/edu_pub/sealert/sea20.html***
4. Joint Commission on Accreditation of Healthcare Organizations. Inside the Joint Commission. Online [newsletter] August 6, 2001. Oakbrook Terrace, IL: CJD-Guidelines for Suspected CJD Cases in Operating Rooms.
5. Muscarella L. "Assessing the risk of Creutzfeldt-Jakob disease." Infection Control Today [online]. August 28, 2001. ***www.infectioncontroltoday.com/articles/181feat1.html***
6. Reichert M, & Schultz J. CJD instrument processing. OR Manager. 2001;17(7):21-22.
7. Roos R. "Overblown fears about CJD lead to over-the-top sterilization recommendation, expert says." IcanPrevent. [online] April 3, 2001. (subscription service, password required) ***www.icanprevent.com***
8. Rosenmann H, et al. "Detection of 14-3-3 protein in the CSF of genetic Creutzfeldt-Jakob disease." *Neurology.* 1997;49(2):593-595.
9. Rutala W & Weber D. "Creutzfeldt-Jakob Disease: Recommendations for disinfection and Sterilization." *Clinical Infectious Diseases.* 2001;32:1348-1356.
10. Steelman V. "Prion Diseases-An evidence-based protocol for infection control." *AORN Journal.* 1999;69(5):946-967.
11. "Prion." Microsoft Encarta Encyclopedia 2000 [CD ROM]. Microsoft Corp. Redmond, WA.
12. New Variant CJD (nvCJD) BSE Info Resource. March 2002. National Cattlemen's Beef Association and Cattlemen's Beef Board. ***www.bseinfo.org/resource/vcjd_fact.htm*** Accessed 1/4/02
13. Pruisner SB. "The Prion Diseases." Scientific American [online]. August 1996. ***www.sciam.com/0896issue/prion/html*** Accessed 1/4/02
14. Archer-Evans S, Boske A, Hodges C. Prions and Mad Cow Disease [web site]. University of Texas-Austin. ***www.esb.utexas.edu/palmer/bio303/group23/Prions%20and%20Mad%20Cow%20Disease.html*** Accessed 11/8/2001
15. "CJD Info." Creutzfeldt-Jakob Disease Foundation Inc. ***cjdfoundation.org/CJDInfo.html*** Accessed 11/8/2001
16. NINDS Transmissible Spongiform Encephalopathies Information Page. National Institute of Neurological Disorders and Stroke. ***www.ninds.nih/gov/health_and_medical/disorders/tse.htm*** Accessed 3/12/02
17. "WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies: Report of a WHO Consultation, Geneva, Switzerland, 23-26 March 1999." National Center for Infectious Diseases. ***www.cdc.gov/ncidod/diseases/cjd/cjd_inf_ctrl_qa.htm#whoguidelines*** Accessed 3/13/02