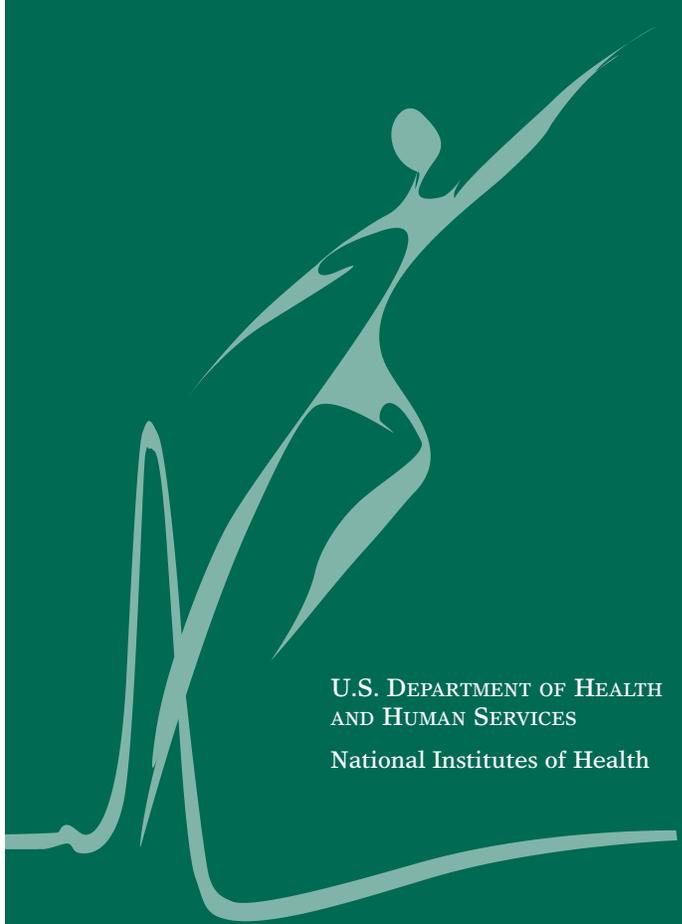
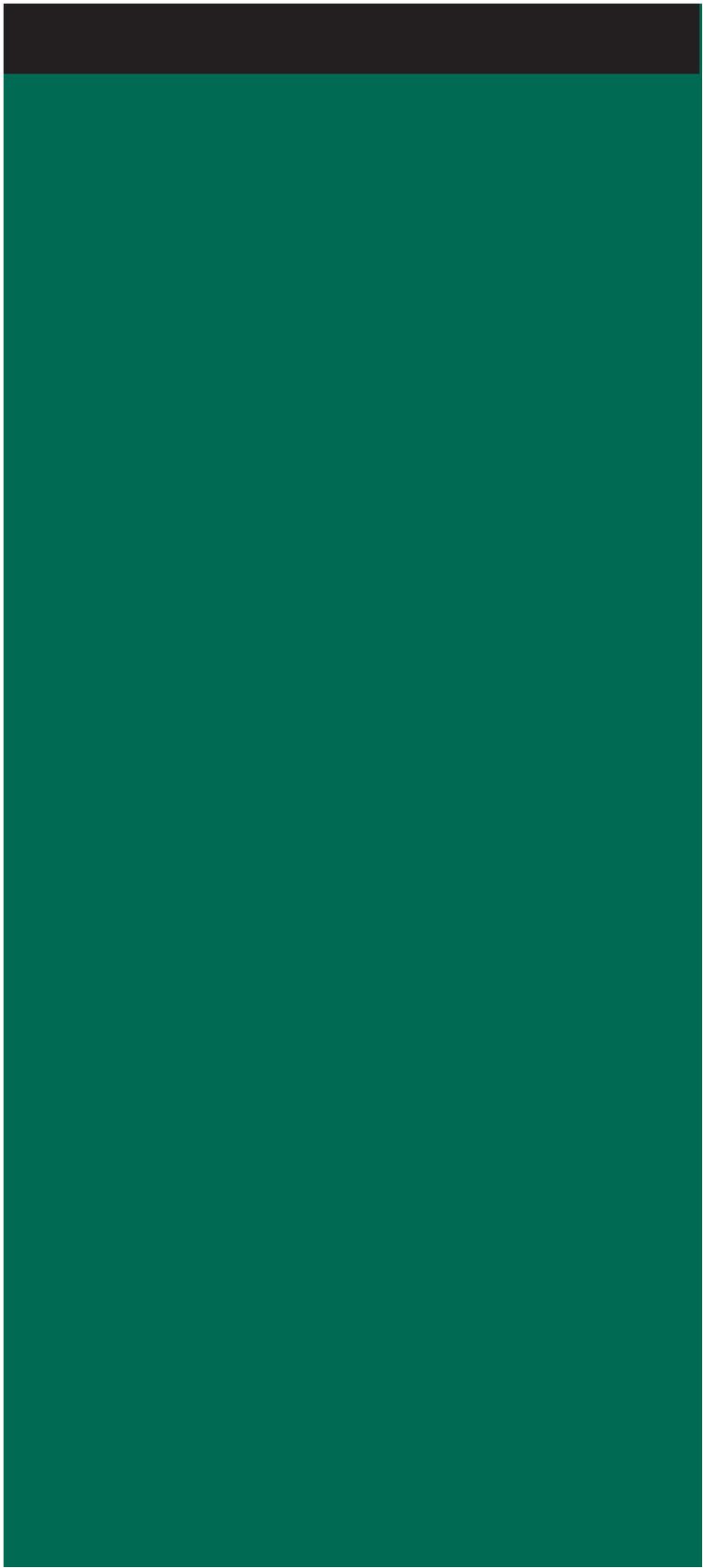


Creutzfeldt-Jakob Disease



U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES

National Institutes of Health



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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 at about age 60, and about 90 percent of patients die within 1 year. In the early stages of the disease, patients 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.

There are three major categories of CJD:

- 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.
- 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.

- 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. 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.

What are the symptoms of the disease?

CJD is characterized by rapidly progressive dementia. Initially, patients 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, the patients' mental impairment becomes severe. They 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 patients and can lead to death.

There are several known variants of CJD. These variants differ somewhat in the symptoms and course of the disease. For example, a variant form of the disease—called new variant or variant (nv-CJD, v-CJD), described in Great Britain and France—begins primarily with psychiatric symptoms, affects younger patients than other types of CJD, and has a longer than usual duration from onset of symptoms to death. Another variant, called the panencephalopathic form, occurs primarily in Japan and has a relatively long course, with symptoms often progressing for several years. Scientists are trying to learn what causes these variations in the symptoms and course of the disease.

Some symptoms of CJD can be similar to symptoms of other progressive neurological disorders, such as Alzheimer's or Huntington's disease. However, CJD causes unique changes in brain tissue which can be seen at autopsy. It also tends to cause more rapid deterioration of a person's abilities than Alzheimer's disease or most other types of dementia.

How is CJD diagnosed?

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. 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 patient, 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 patient, 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.*

How is the disease treated?

There is no treatment that can cure or control CJD. Researchers have tested many drugs, including amantadine, steroids, interferon, acyclovir, antiviral agents, and antibiotics. *Studies of a variety of other drugs are now in progress. However, so far none of these treatments has shown any consistent benefit in humans.*

Current treatment for CJD is aimed at alleviating symptoms and making the patient as comfortable as possible. Opiate drugs can help relieve pain if it occurs, and the drugs clonazepam and sodium valproate may help relieve myoclonus. During later stages of the disease, changing the person's position frequently can keep him or her comfortable and helps prevent bedsores. A catheter can be used to drain urine if the patient cannot control bladder function, and intravenous fluids and artificial feeding also may be used.

What causes CJD?

Some researchers believe an unusual "slow virus" or another organism causes CJD. However, they have never been able to isolate a virus or other organism in people with the disease. Furthermore, the agent that causes CJD has several characteristics that are unusual for known organisms such as viruses and bacteria. It is difficult to kill, it does not appear to contain any genetic information in the form of nucleic acids (DNA or RNA), and it usually has a long

incubation period before symptoms appear. In some cases, the incubation period may be as long as 40 years. The leading scientific theory at this time maintains that CJD and the other TSEs are caused by a type of protein called a *prion*.

Prion *proteins* occur in both a normal form, which is a harmless protein found in the body's cells, and in an infectious form, which causes disease. The harmless and infectious forms of the prion protein *have the same sequence of amino acids (the "building blocks" of proteins)* but the infectious form of the protein takes a different folded shape than the normal protein. Sporadic CJD may develop because some of a person's normal prions spontaneously change into the infectious form of the protein and then alter the prions in other cells in a chain reaction.

Once they appear, abnormal prion proteins *aggregate, or clump together. Investigators think these protein aggregates may lead to the neuron loss and other brain damage seen in CJD. However, they do not know exactly how this damage occurs.*

About 5 to 10 percent of all CJD cases are inherited. These cases arise from a mutation, or change, in the gene that controls formation of the normal prion protein. While prions themselves do not contain genetic information and do not require genes to reproduce themselves, infectious prions can arise if a mutation occurs in the gene for the body's normal

prion *protein*. If the prion *protein* gene is altered in a person's sperm or egg cells, the mutation can be transmitted to the person's offspring. Several different mutations in the prion gene have been identified. The particular mutation found in each family affects how frequently the disease appears and what symptoms are most noticeable. However, not all people with mutations in the prion *protein* gene develop CJD.

How is CJD transmitted?

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 and spinal cord fluid from infected patients 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.

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 the prions causing BSE and v-CJD, there is no direct proof to support this theory. Furthermore, BSE has never been found in the United States, and importation of cattle and beef from countries with BSE has been banned in the United States since 1989 to reduce the risk that it will occur in this country.

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. 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.

How can people avoid spreading the disease?

To reduce the already very low risk of CJD transmission from one person to another, people should never donate blood, tissues, or organs if they have suspected or confirmed CJD, or if they are at increased risk because of a family history of the disease, a dura mater graft, or other factor.

Normal sterilization procedures such as cooking, washing, and boiling do not destroy prions. Caregivers, health care workers, and undertakers should take the following precautions when they are working with a person with CJD:

- Cover cuts and abrasions with waterproof dressings.

- Wear surgical gloves when handling a patient's tissues and fluids or dressing the patient's wounds.
- Avoid cutting or sticking themselves with instruments contaminated by the patient's blood or other tissues.
- Use disposable bedclothes and other cloth for contact with the patient. If disposable materials are not available, regular cloth should be soaked in undiluted chlorine bleach for an hour or more, then washed in a normal fashion after each use.
- Use face protection if there is a risk of splashing contaminated material such as blood or cerebrospinal fluid.
- Soak instruments that have come in contact with the patient in undiluted chlorine bleach for an hour or more, then use an autoclave (pressure cooker) to sterilize them in distilled water for at least one hour at 132-134 degrees Centigrade.

Fact sheets listing additional precautions for healthcare workers and morticians are available from the NINDS and the World Health Organization.

What research is taking place?

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.

How can I help research?

Scientists are conducting biochemical analyses of brain tissue, blood, spinal fluid, urine, and serum in hope of determining the nature of the transmissible agent or agents causing CJD. To help with this research, they are seeking biopsy and autopsy tissue, blood, and cerebrospinal fluid from patients with CJD and related diseases. The following investigators have expressed an interest in receiving such material:

Dr. Pierluigi Gambetti, Director
National Prion Disease Pathology
Surveillance Center
Institute of Pathology
Room 419, Case Western Reserve University
2085 Adelbert Road
Cleveland, OH 44106
(216) 368-0587
Fax: (216) 368-4090
cjdsurv@cwru.edu
www.cjdsurveillance.com/

Dr. Laura Manuelidis

Yale University School of Medicine
Section of Neuropathology
310 Cedar Street
New Haven, Connecticut 06510
(203) 785-4442

Dr. Stephen DeArmond or

Dr. Stanley Prusiner

Department of Pathology/
Neuropathology Unit
HSW 430
University of California, San Francisco
San Francisco, California 94143
(415) 476-5236

Where can I get help?

The following organizations can provide information and support for people and families affected by Creutzfeldt-Jakob disease:

Creutzfeldt-Jakob (CJD) Foundation

P.O. Box 5312
Akron, Ohio 44334
(800) 659-1991
www.cjdfoundation.org

National Organization for Rare Disorders

P.O. Box 1968
Danbury, Connecticut 06813-1968
(203) 744-0100
(800) 999-6673 (voicemail only)
www.rarediseases.org

Alzheimer's Association

919 North Michigan Avenue
Suite 1100
Chicago, Illinois 60611-1676
(312) 335-8700
(800) 272-3900
www.alz.org

**Alzheimer's Disease Education
and Referral Center**

P.O. Box 8250
Silver Spring, Maryland 20907-8250
(301) 495-3311
(800) 438-4380
www.alzheimers.org

**National Hospice and Palliative
Care Organization**

1700 Diagonal Road, Suite 625
Alexandria, Virginia 22314
(703) 837-1500
(800) 658-8898
www.nhpco.org

National Family Caregivers Association

10400 Connecticut Avenue, Suite 500
Kensington, Maryland 20895-3944
(301) 942-6430
(800) 896-3650
www.nfcacares.org

Family Caregiver Alliance

690 Market Street, Suite 600
San Francisco, California 94104
(415) 434-3388
(800) 445-8106 (in California)
www.caregiver.org

Well Spouse Foundation

63 West Main Street
Freehold, New Jersey 07728
(732) 577-8899
(800) 838-0879
www.wellspouse.org

Centers for Disease Control and Prevention

1600 Clifton Road, NE
Atlanta, Georgia 30333
(404) 639-3311
(800) 311-3435
www.cdc.gov

If you are interested in learning more about steps taken to ensure the safety of beef and other agricultural products in the United States, contact:

**United States Department of
Agriculture (USDA)**

National Agricultural Library
10301 Baltimore Avenue
Beltsville, Maryland 20705-2351
(301) 504-5755
www.usda.gov

For information on the safety of medical products and procedures, contact:

Food and Drug Administration

5600 Fishers Lane
Rockville, Maryland 20857
(301) 827-4573
www.fda.gov

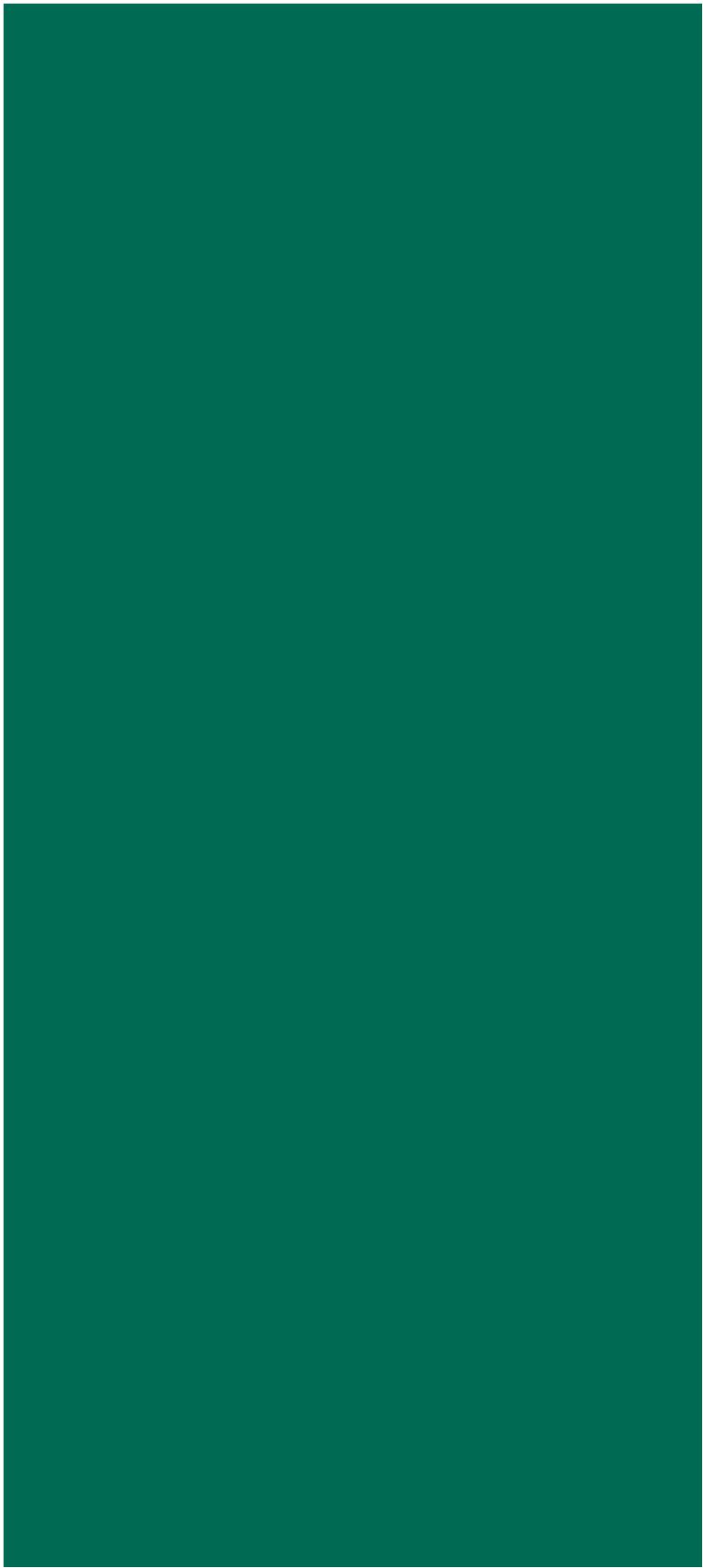
Health care workers who wish to receive information on special surgical and disinfection procedures should see the NINDS Fact Sheet for Healthcare Workers and Morticians or contact the NINDS Brain Resources and Information Network (BRAIN) at:

BRAIN

P.O. Box 5801
Bethesda, Maryland 20824
(800) 352-9424
www.ninds.nih.gov

The World Health Organization

Office at the United Nations
2, United Nations Plaza
New York, New York 10017
(212) 963-4388
(800) 877-2693, ext. 118
www.who.int





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