Prion disease

Prion disease represents a group of conditions that affect the nervous system in humans and animals. In people, these conditions impair brain function, causing changes in memory, personality, and behavior; a decline in intellectual function (dementia); and abnormal movements, particularly difficulty with coordinating movements (ataxia). The signs and symptoms of prion disease typically begin in adulthood and worsen with time, leading to death within a few months to several years.

Frequency

These disorders are very rare. Although the exact prevalence of prion disease is unknown, studies suggest that this group of conditions affects about one person per million worldwide each year. Approximately 350 new cases are reported annually in the United States.

Causes

Between 10 and 15 percent of all cases of prion disease are caused by mutations in the \( PRNP \) gene. Because they can run in families, these forms of prion disease are classified as familial. Familial prion diseases, which have overlapping signs and symptoms, include familial Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker syndrome (GSS), and fatal familial insomnia (FFI).

The \( PRNP \) gene provides instructions for making a protein called prion protein (PrP). Although the precise function of this protein is unknown, researchers have proposed roles in several important processes. These include the transport of copper into cells, protection of brain cells (neurons) from injury (neuroprotection), and communication between neurons. In familial forms of prion disease, \( PRNP \) gene mutations result in the production of an abnormally shaped protein, known as \( \text{PrP}^\text{Sc} \), from one copy of the gene. In a process that is not fully understood, \( \text{PrP}^\text{Sc} \) can attach (bind) to the normal protein (\( \text{PrP}^\text{C} \)) and promote its transformation into \( \text{PrP}^\text{Sc} \). The abnormal protein builds up in the brain, forming clumps that damage or destroy neurons. The loss of these cells creates microscopic sponge-like holes (vacuoles) in the brain, which leads to the signs and symptoms of prion disease.

The other 85 to 90 percent of cases of prion disease are classified as either sporadic or acquired. People with sporadic prion disease have no family history of the disease and no identified mutation in the \( PRNP \) gene. Sporadic disease occurs when \( \text{PrP}^\text{C} \) spontaneously, and for unknown reasons, is transformed into \( \text{PrP}^\text{Sc} \). Sporadic forms of prion disease include sporadic Creutzfeldt-Jakob disease (sCJD), sporadic fatal insomnia (sFI), and variably protease-sensitive prionopathy (VPSPr).
Acquired prion disease results from exposure to PrPsc from an outside source. For example, variant Creutzfeldt-Jakob disease (vCJD) is a type of acquired prion disease in humans that results from eating beef products containing PrPsc from cattle with prion disease. In cows, this form of the disease is known as bovine spongiform encephalopathy (BSE) or, more commonly, "mad cow disease." Another example of an acquired human prion disease is kuru, which was identified in the South Fore population in Papua New Guinea. The disorder was transmitted when individuals ate affected human tissue during cannibalistic funeral rituals.

Rarely, prion disease can be transmitted by accidental exposure to PrPsc-contaminated tissues during a medical procedure. This type of prion disease, which accounts for 1 to 2 percent of all cases, is classified as iatrogenic.

Inheritance Pattern

Familial forms of prion disease are inherited in an autosomal dominant pattern, which means one copy of the altered PRNP gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the altered gene from one affected parent. In some people, familial forms of prion disease are caused by a new mutation in the gene that occurs during the formation of a parent's reproductive cells (eggs or sperm) or in early embryonic development. Although such people do not have an affected parent, they can pass the genetic change to their children.

The sporadic, acquired, and iatrogenic forms of prion disease, including kuru and variant Creutzfeldt-Jakob disease, are not inherited.

Other Names for This Condition

- inherited human transmissible spongiform encephalopathies
- prion-associated disorders
- prion-induced disorders
- prion protein diseases
- transmissible dementias
- transmissible spongiform encephalopathies
- TSEs

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
• Genetic Testing Registry: Genetic prion diseases

• Genetic Testing Registry: Gerstmann-Straussler-Scheinker syndrome

• Genetic Testing Registry: Jakob-Creutzfeldt disease

• Genetic Testing Registry: Kuru, susceptibility to

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22prion+disease%22+OR+%22Creutzfeldt-Jakob+disease%22+OR+%22Gerstmann-Straussler-Scheinker+syndrome%22+OR+%22fatal+familial+insomnia%22

Other Diagnosis and Management Resources
• Creutzfeldt-Jakob Disease Foundation: Caregiving Ideas
  https://cjdfoundation.org/caregiving

• GeneReview: Genetic Prion Diseases
  https://www.ncbi.nlm.nih.gov/books/NBK1229

• MedlinePlus Encyclopedia: Creutzfeldt-Jakob disease
  https://medlineplus.gov/ency/article/000788.htm

• MedlinePlus Encyclopedia: Kuru
  https://medlineplus.gov/ency/article/001379.htm

Additional Information & Resources
Health Information from MedlinePlus
• Encyclopedia: Creutzfeldt-Jakob disease
  https://medlineplus.gov/ency/article/000788.htm

• Encyclopedia: Kuru
  https://medlineplus.gov/ency/article/001379.htm

• Health Topic: Creutzfeldt-Jakob Disease
  https://medlineplus.gov/creutzfeldtjakobdisease.html

• Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html

• Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
Genetic and Rare Diseases Information Center

- Creutzfeldt-Jakob disease

- Gerstmann-Straussler-Scheinker disease

- Variant Creutzfeldt-Jakob disease

Additional NIH Resources

- National Institute of Allergy and Infectious Diseases: Prion Diseases
  https://www.niaid.nih.gov/diseases-conditions/prion-diseases

- National Institute of Neurological Disorders and Stroke: Creutzfeldt-Jakob Disease Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Creutzfeldt-Jakob-Disease-Information-Page

- National Institute of Neurological Disorders and Stroke: Gerstmann-Straussler-Scheinker Disease Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Gerstmann-Straussler-Scheinker-Disease-Information-Page

- National Institute of Neurological Disorders and Stroke: Kuru Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Kuru-Information-Page

- National Institute of Neurological Disorders and Stroke: Transmissible Spongiform Encephalopathies Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Transmissible-Spongiform-Encephalopathies-Information-Page

Educational Resources

- Centers for Disease Control and Prevention: About Prion Diseases
  https://www.cdc.gov/prions/

- Johns Hopkins Medicine: Prion Diseases
  https://www.hopkinsmedicine.org/health/conditions-and-diseases/prion-diseases

- MalaCards: prion disease
  https://www.malacards.org/card/prion_disease

- Merck Manual Home Edition for Patients and Caregivers

- Orphanet: Fatal familial insomnia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=466
• Orphanet: Gerstmann-Straussler-Scheinker syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=356
• Orphanet: Human prion disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=56970
• Orphanet: Sporadic Creutzfeldt-Jakob disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=204
• University of California, San Francisco Memory and Aging Center
  https://memory.ucsf.edu/dementia/rapidly-progressive-dementias/prion-diseases
• World Health Organization: Prion Diseases
  https://www.who.int/zoonoses/diseases/prion_diseases/en/

Patient Support and Advocacy Resources
• Alzheimer's Association: Creutzfeldt-Jakob Disease
  https://www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/
  creutzfeldt-jakob-disease
• Contact a Family (UK): Creutzfeldt-Jakob Disease
  https://contact.org.uk/medical-information/conditions/c/creutzfeldt-jakob-disease/
• Creutzfeldt-Jakob Disease Foundation
  https://cjdfoundation.org/
• National Organization for Rare Disorders (NORD): Creutzfeldt-Jakob Disease
  https://rarediseases.org/rare-diseases/creutzfeldt-jakob-disease/
• National Prion Disease Pathology Surveillance Center
  https://case.edu/medicine/pathology/divisions/prion-center/
• The UK Creutzfeldt-Jakob Disease Surveillance Unit
  http://www.cjd.ed.ac.uk/

Clinical Information from GeneReviews
• Genetic Prion Diseases
  https://www.ncbi.nlm.nih.gov/books/NBK1229

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Prion+Diseases%5BMAJR%5D%29+AND+%28%28prion+disease%5BTIAB%5D%29+OR+%28Creutzfeldt-Jakob+disease%5BTIAB%5D%29+OR+%28fatal+familial+insomnia%5BTIAB%5D%29+OR+%28Gerstmann-Straussler-Scheinker+syndrome%5BTIAB%5D%29%29+AND+english%5Bmh%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D
Catalog of Genes and Diseases from OMIM

• CREUTZFELDT-JAKOB DISEASE  
  http://omim.org/entry/123400

• FATAL FAMILIAL INSOMNIA  
  http://omim.org/entry/600072

• GERSTMANN-STRAUSSLER DISEASE  
  http://omim.org/entry/137440

• KURU, SUSCEPTIBILITY TO  
  http://omim.org/entry/245300

Sources for This Summary

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22196171  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3296552/

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11357156

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22710755

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