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The review on: "Creutzfeldt-Jakob disease"

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Abstract

This review will explore the information about Creutzfeldt -Jakob disease (CJD), which is the human prion disease. CJD is a rare brain disorder and rapidly progressive. CJD belongs to the family of human prion disease, which is caused by misfolded, transmissible infections particles, or prions. Transmissible spongiform encephalopathy (TSEs), also known as prion disease. Spongiform refers to the characteristic appearance of infected brains. CJD affects about one person in every one million people per year worldwide. CJD is a fatal neurodegenerative disorder which is having a higher mortality rate. CJD usually appears in later life and has a high incubation period but become rapidly progressive once clinically symptoms begin. CJD exist in three major groups sporadic CJD (sCJD), Acquired CJD, and Genetic CJD. The sporadic form generally affects the late middle age or elderly persons (Mean age of 67 years). Most people with clinically diagnosed CJD die within a year. Other neurodegenerative illness like Alzheimer's disease involves the deposition of an aberrantly folded protein: although CJD is transmissible. There is no specific treatment for CJD except for supportive care. The arrangement of different clinicians and surveillance programs can maintain awareness of CJD to control the future incidence of its transmission.

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INTRODUCTION

The term "Prion" was coined by Stanley B. Prusiner in 1982, which is derived from proteinaceous infectious particles [1]. Prion illness was previously known as transmissible spongiform encephalopathy [2]. Human prion protein primarily presents in the nervous system but also in other tissues throughout the body. The prion group is related to neurodegenerative disorders, which affect both humans and animals. Prion disease mostly has a high incubation period but typically become rapidly progressive once clinically symptoms begin. Prion disease can be inherited, can occur sporadically and can be infectious and affects healthy living persons. The prion protein is the major pathogen in prion disease. Prion disease can be acquired, sporadic and hereditary in the human population, depending on the severity of the illness [3] (Table 1).

CJD is the most frequently seen type of prion disease. CJD is a neurological disease that is swiftly progressing, fatal, and transmissible because it is caused by an aberrant protein known as a prion. The discovery of the prion disease was associated with the conversion of normal prion protein (PrP^{c}) to misfolded form (PrP^{sc}). In the 1920s, Creutzfeldt and Alfons independently described a syndrome characterized by progressive ataxia, tremor, dementia, and death [4]. In 1922, Spielmeyer used the term CJD to characterise the illness first described by two Ger-

man physicians in their work [5]. The clinical course of CJD is swift and always fatal. Having more mortality rate makes it one of the dangerous disorders. About 70 percent of people clinically diagnosed with CJD die within a year [6]. CJD has a 100% mortality rate and is typically seen in people after 60 years of age.

Sporadic CJD acquired CJD (iatrogenic CJD, Variant CJD), and familial CJD are all subtypes of CJD. All the types of CJD are transmissible. Sporadic CJD is the most common form of prion disease in humans, with psychiatric symptoms often accompanying neurological abnormalities. While sporadic CJD is a rare cause of dementia in middle-aged and older people, the iatrogenic and variant types of CJD are more common in younger individuals. The cause of (sCJD) is unknown. Inherited cases of CJD associated with the mutation of the prion protein gene (PRNP) and acquired form are caused by the transmission of infection from human to human or, as a zoonosis, from cattle to Human [7]. Symptoms of CJD are Dementia, myoclonus, ataxia, cortical blindness etc. A patient's memory may decline, their behaviour may change, they may lose their coordination, and their vision may be affected [8]. CJD is often a diagnostic challenge for physicians, and there are several tests that can help to diagnose CJD, including electroencephalography (EEG), Magnetic brain resonance imaging (MRI), genetic testing etc. CJD can only be diagnosed through a brain biopsy or autopsy. The gold standard for diagnosis is a brain biopsy. CJD is a disease for which there is no cure. Symptomatic and supportive treatment is the primary mode of intervention.

PATHOPHYSIOLOGY OF CJD

CJD is caused by prions or transmissible infectious particles. The concentration of CJD prions in infected patients or in Individuals vary throughout the body but is mainly high in the brain and posterior eye (retina and optical nerve) [9]. The normal protein can become infected or misfolded prion by factors like a mutation in prion gene, infection of nerves tissue and heredity transmission of infected prions. Neurodegeneration characterised by the spongiform brain and clinical symptoms like paranoia, dementia, myoclonus, etc., is caused by the accumulation of misfolded prions in the brain. For the pathophysiology of CJD, CJD is caused by prions. PrP^{c} is found in the cell membrane of the normal brain. PrP is a normal cellular protein which function is not specific. In humans, PrP protein is encoded by the PrP gene (PRNP), which is located on chromosome 20 [10]. The pathological event in this is a formation of abnormal PrP^{sc} from the cellular form of PrP^{sc}. Scrapie prion protein (PrPsc) means the Alternation of naturally existing prion protein (PrP^{c}) to an abnormal folded protein [11]. Both PrP^{c} and PrP^{sc} forms have an identical amino acid sequence, but the posttranslational changes cause, PrP^{c} (40% alpha-helix) to misfold to form PrP^{sc} (45% beeta sheet) [12]. PrP^{c} and PrP^{sc} both have different physicochemical properties. (Figure 1)

TYPES OF CJD

CJD is classified into the following types:-

1. Sporadic CJD (sCJD)
2. Familial CJD or Inherited CJD
3. Variant CJD (vCJD)
4. Iatrogenic CJD (iCJD)

Sporadic CJD (sCJD)

Symptoms of Sporadic CJD include rapidly deteriorating dementia, cerebral ataxia, akinetic mutism, and visual impairment. There are around 1-2 deaths per million people per year from sporadic CJD. sCJD accounts for 85% of CJD cases [13]. sCJD has been detected in Europe, North America, Australia etc. precise cause of sCJD is unclear, but results from the random structural changes in the normal PrP protein causing the formation of PrP^{sc} or somatic mutation in the PRNP gene. sCJD is a very rapid disease which means survival is 6 months. The peak incidence of sCJD is in the 7^{th}decade of life; 90% patients of with sCJD die within a year. Cases of younger people (20-the 40s) or older (>80) are less common [14]. PrP gene polymorphism codon 129, which codes for either valine or methionine, and the Type 1 or Type 2 of an aberrant isoform of PrPsc in the brain, are used to classify sCJD. They are unique in terms of their physical and chemical characteristics [15]. The six molecular subtypes are based on the criteria listed above. Sporadic CJD has been classified according to its molecular and clinical characteristics (MM1, MM2, MV1, MV2, VV1 OR VV2). MM2C and MM2T are two distinct subtypes of MM2 based on histological criteria [16].

Familial or Inherited

Familial CJD is a kind of prion disease that is passed down from generation to generation. The first familial case of CJD was recorded in 1924 by Kirschbaum [17]. Familial CJD accounts for approximately 10% of cases of prion disease. A variety of mutations in the PRNP gene have been

Table 1: Classification of human prion disease

Groups	Subgroups
Acquired	Kuru Variant CJD Iatrogenic CJD
Familial (10%-15%)	Genetic CJD Fatal familial insomnia Gerstmann-straus-sler-Scheinker disease
Idiopathic (85%)	Sporadic CJD Sporadic fatal insomnia Variably protease-sensitive prionopathy

Note:
Mortality rate- the mortality rate is the measure of the number of deaths in a particular amount of population per unit time.
Zoonosis- A disease can be transmitted to humans from animals.

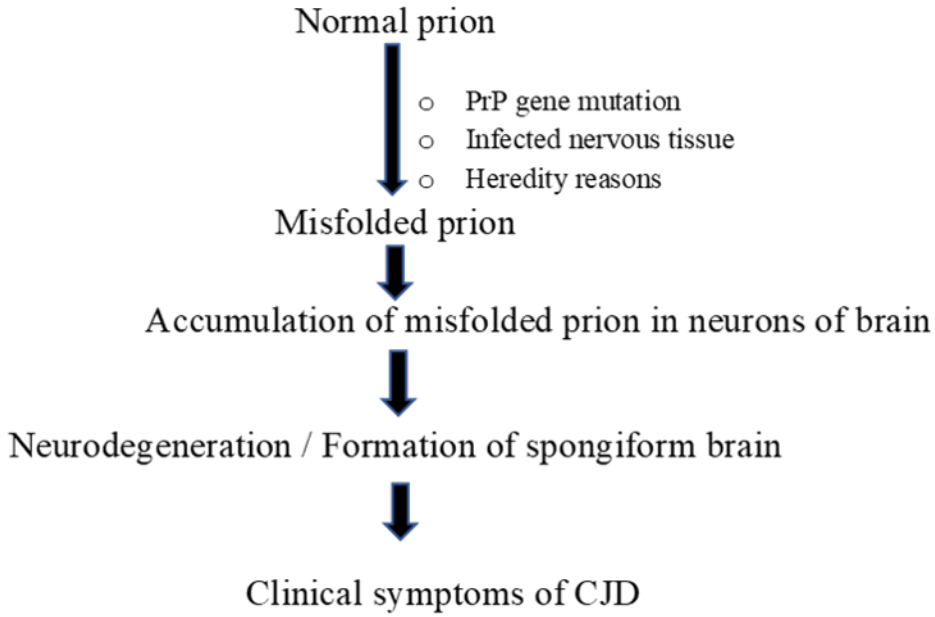

Figure 1: Pathophysiology of the Creutzfeldt-Jakob Disease (CJD)

linked to familial CJD, which is believed to be directly pathogenic. Family CJD is passed down through autosomal dominant transmission, with a high degree of penetrance. CJD is caused by a genetic mutation in cases of familial CJD. The course of the disease varies from several months to years. Fatal familial insomnia (FFI), Gerstmann-straussler-scheinker (GSS) and fCJD have historically been classified as three distinct phenotypes [18]. An autosomal dominant pattern is present in GSS and FFI. In order to develop the disease, you only need to have one mutant copy of the PrP gene. Clinical characterisation alone may not be able to distinguish certain cases of familial CJD from sCJD, but genetic testing of the PRNP locus can often aid. sCJD tends to progress more quickly than fCJD. The combination of the D178N Mutation and methionine at C 129 on the afflicted allele (D178N-129M) causes fatal insomnia [19]. For the most part, it's fatal within two years. GSS syndrome is caused by the P102L mutation in PRNP.

Variant CJD

As of 1996, vCJD was recognised as the rarest human prion disease. It is a result of bovine spongiform encephalopathy in cattle entering human food, or it is a result of eating food contaminated with BSE [20]. The United Kingdom is the country with the highest incidence of Bovine spongiform encephalopathy. In the variant, CJD patients had seen notably young. The median age is 26 years, contrasting the age distribution of sporadic CJD. However, an older individual has been affected. This disease has specific neuropathology, with florescent plaques in

the brain, widespread deposition of abnormal PrP, and thalamic gliosis in the brain (Figure 2). The mean survival time of vCJD patients is 14 months, but some patients have survived > 3 years after the onset of symptoms [21]. It's also possible for vCJD to be transmitted by blood transfusion; three cases of vCJD have occurred in individuals in the UK who received non-leucodepleted red blood cells from asymptomatic UK donor who subsequently died from vCJD after donation. All three cases were methionine homozygotes (MM) at codon 129 in the PRNP gene.

Iatrogenic CJD

Iatrogenic CJD was first described in 1974 in patients who had received a transplant of corneal tissue from an infected cadaver. Iatrogenic CJD is most likely to sporadic CJD. Iatrogenic CJD is transmitted from one person to another by medical or surgical treatment. Based on the identification of relevant preceding procedures, diagnosis of iCJD can be done. Dura matter grafts with contaminated materials led to more than 60 cases of CJD, which an incubation period is lasting between 1 to 14 years. The two principal aetiologies for iatrogenic CJD are treatment with cadaveric pituitary-derived growth hormone (c-hGH) and human dura matter (hDM) grafts. The hDM associated iCJD epidemic began in 1985 and peaked globally in 1997 [19]. The largest number of hDM associated iCJD cases were found in Japan [22], where high grafting procedures were performed like in other countries. Also, cases were reported in Asian nations, Europe, USA, Australia, South Africa. The hGH associated iCJD was most frequently found in France, the UK, and the USA and less commonly in other European countries. This epidemic began in 1984 and peaked globally in 1995 [19].

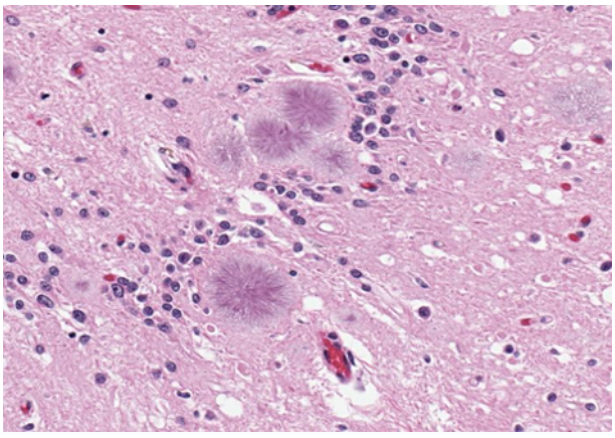

Figure 2: A stained and magnified slice of brain tissues shows the presence of typical amyloid plaques found in the case of vCJD

CAUSES

CJD is a type of human prion disease. CJD is caused by an abnormal transmissible protein known as prions. Prions are responsible for CJD. Prions are healthy protein that has changed their shape. This damage to the brain tissue and causes the symptoms of CJD. In some cases, CJD causes sporadically and in some cases may be inherited or acquired.

1. The precise cause of sporadic CJD is unclear, but the studies result from the random structural changes in normal PrP protein causing the formation of PrP^{sc} or somatic mutation in the gene.
2. Inherited CJD is caused by the mutation in the PRNP gene, which is believed to be directly pathogenic.
3. Variant CJD caused due to consumption of food contaminated with BSE. Consumption of infected blood or plasma transfusion
4. Iatrogenic CJD is caused due to prion transmission during a medical procedure, surgical treatment. Procedure including corneal transplantation, implantation of human dura matter, or parenteral treatment with human cadaveric pituitary extracts [23].

SYMPTOMS

Each group of CJD has recorded a variety of psychiatric and neurological symptoms. Dementia is the most common clinical sign of the condition. Additionally, there are a number of clinical symptoms that are found: As the condition progresses, symptoms such as myoclonus, ataxia, visual changes leading to cortical blindness and akinetic mutism is seen in the last stage of the disease. [3]. (Table 2)

1. Sporadic CJD – In sporadic CJD, symptoms mainly affect the working of the nervous system (neurological symptoms). Most frequently, sleep disturbance, insomnia, hypersomnolence. Psychotic symptoms such as delusions, paranoia, disorganized speech, behaviour as well as a hallucination.
2. Variant CJD - In vCJD, psychiatric symptoms appear almost immediately about 85% of the time. Comparatively, in about 40% of the cases of CJD, neurological symptoms appeared at the start. On average first psychiatric symptoms occurred at zero months, and neurological symptoms occurred at the two months from the onset [24]. In Less than 4 months of the

Table 2: World health criteria for the diagnosis of sCJD

World health organization criteria for the diagnosis of Sporadic CJD		
I		Progressive dementia
II		
	A	Myoclonus
	B	Visual or cerebellar disturbance
	C	Pyramidal or extrapyramidal features
	D	Akinetic mutism
III		
	A	Typical EEG
	B	Positive CSF 14-3-3 protein

Possible CJD: I and at least 2/4 of II and duration <2 years
Probable CJD: I and at least 2/4 of II and at least 1/2 of III and duration <2 years
Definite CJD: Neuropathologically confirmed diagnosis

vCJD, common psychiatric symptoms included depression, anxiety, irritability, insomnia, and loss of interest. Between 4 to 6 months, poor memory, impaired concentration and aggregation were common. Eventually, in this condition patient may lose the ability to move or speak; therefore 24 hours nursing care after that death occurs approximately a year after the onset of symptoms.

3. Familial CJD – The symptoms of fCJD may vary depending upon the type of mutation involved [25]. fCJD is present in neuropsychiatric symptoms. fCJD has the same pattern like sCJD, but it often takes a longer duration for the progression of symptoms. From months to years. Early symptoms of fCJD maybe like mood swings, depression, memory lapses, and lack of interest.

RISK FACTORS

Here are some risk factors that seem to be associated with different types of CJD.

1. Age- sCJD is a type of CJD that tends to occur later in life, usually around 60. Normally, vCJD has affected younger people, usually at the 20s and Familial CJD appears slightly earlier.

2. Genetic- Familial CJD cases have a mutation that causes the disease.

3. Exposure to the contaminated tissue.

DIAGNOSIS

There are certain supportive tests for the probable diagnosis of CJD: Electroencephalography (EEG), Lumber punches, magnetic resonance imaging (MRI), lumber punches, blood test, brain biopsy, tonsil biopsy. Brain biopsy is the only way to confirm the diagnosis of CJD.

1. Electroencephalography- Brain's electrical activity can be measured by using an instrument called electroencephalography (EEG). Because PSWCs (periodic sharp wave complexes) are observed in roughly 80% of sCJD cases, they have been included in the likely sCJD diagnostic criteria [26]. This is because PSWCs are not frequent in other subtypes. Patients with the MM1 and MV1 genotypes are more likely to develop these complexes than those with the valine homozygous variation at codon 129 [27]. For diagnosing CJD, EEG is one of the most useful tools at the moment.

2. Magnetic Resonance Imaging- MRI type of scan produces an image of the brain. MRI has played an increasingly important role in the diagnosis of CJD cases since basal ganglia abnormalities on T2- weighted have been described [27]. The newer technological advancement in MRI enabled physicians to use FLAIR, and diffusion-weighted imaging (DWI), Apparent diffusion coefficient [28]. In current DMI has also been proven to be a valuable diagnostic tool.

3. Lumber Puncture (Spinal Tap)- In lumber puncture, a sample of cerebrospinal fluid (CSF)

is taken by inserting a hollow needle into the lower part of the spinal column. The spinal fluid is analysed for the presence of protein biomarkers such as 14-3-3 protein, microtubule-associated protein tau and S100B protein [29]. The 14-3-3 protein is detectable in 90% of patients with typical CJD. This test is more accurate over 95% in detecting sporadic CJD cases.

4. Brain biopsy- In brain biopsy sample of tissue is usually removed from the frontal lobe in the brain by neurosurgical procedures such as brain operation. Brain biopsy is able to give pathological confirmation of the disease and is considered the gold standard for diagnosis [30]. Brain biopsy is not routinely done because it poses a possible risk to the patient and the medical team performing the surgery.

Blood tests and other biochemical tests are normal in CJD testing. The tonsil biopsy may be useful for the diagnosis of vCJD because only in vCJD cases infectivity can be seen in tonsil tissue.

TREATMENT

CJD has no effective treatment, thus identifying risk factors and delaying disease progression are critical. There is no cure for CJD, and there is no medication available for controlling it and showing its progression. Research is needed the better define symptoms as well as for effective treatments [31]. Some drugs can help to treatment symptomatically, for example, clonazepam for the treatment of myoclonus.

PREVENTION

Despite the fact that CJD is so rare, it is extremely difficult to prevent. Most occur of CJD spontaneously, which has an unknown reason (sporadic CJD), and some are caused due to inheritance. CJD cases that occur due to medical procedures or by eating infected animals can be prevented by taking precautions. Risk of exposure to the vCJD or CJD, safety must be ensuring in the blood bank or while blood transfusion. An efficient sterilization technique should be applied [32].

CONCLUSION

From the above information, we conclude that CJD is a rare, neurodegenerative and fatal disease. CJD is classified within the human prion disorders. A probable diagnosis of CJD is based on a clinical and supportive test (EEG, CSF, MRI), but additional testing and various diagnosis criteria are required for the diagnosis. There is no effective medication for CJD. Currently, doctors are concerned towards the relieve the symptoms of CJD patients. Therefore, CJD needs more research towards the treatment and diagnosis.

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Conflict of Interest

The authors declare that they have no conflict of interest.

REFERENCES

[1] Graeme Mackenzie and Robert Will. Creutzfeldt-Jakob disease: recent developments. *F1000Research*, 6:2053, 2017.

[2] Yaushi lwasaki. Creutzfeldt-Jakob disease. *Neuropathology*, 37(2):174–188, 2017.

[3] Diego Cardoso Fragoso, Augusto Lio da Mota Gonçalves Filho, Felipe Torres Pacheco, et al. Imaging of Creutzfeldt-Jakob Disease: Imaging Patterns and Their Differential Diagnosis. *Neurologic/Head and Neck Imagine*, 37(1):234–257, 2017.

[4] M. da mota Gomes. Creutzfeldt-Jakob disease: one hundred years of participation in the design of the transmissible spongiform encephalopathy. *Rev Bras Neurol*, 53(3):25–28, 2020.

[5] W Spielmeyer. Die histopathologische Forschung in der Psychiatrie. *Klin Wochenschr*, 1(37):1817–1819, 1922.

[6] J Wadsworth, S Joiner, A Hill, et al. Tissue distribution of protease-resistant prion protein in variant Creutzfeldt-Jakob disease using a highly sensitive immunoblotting assay. *The Lancet*, 358(9277):171–180, 2001.

[7] G Robert Will. Acquired prion disease: iatrogenic CJD, variant CJD, kuru. *Br. Med. Bull.*, 66:255–265, 2003.

[8] MW Head. Human prion diseases: molecular, cellular and population biology. *Neuropathology*, 33(3):221–236, 2013.

[9] L Uttley, R Wong, C Carroll, et al. Creutzfeldt-Jakob disease: a systematic review of Global incidence, prevalence, infectivity, and incubation. *The Lancet Infectious Diseases*, 20(1):E2–E10, 2020.

[10] Y C Liao, R V Lebo, G A Clawson, and E A Smuck-

ler. Human prion protein cDNA: molecular cloning, chromosomal mapping, and biological implications. *Science*, 233(4761):364–367, 1986.

[11] Jean Y. Douet, Caroline Lacroux, Naima Aron, et al. Distribution and Quantitative Estimates of Variant Creutzfeldt-Jakob Disease Prions in Tissues of Clinical And Asymptomatic Patients. *Emerging Infectious Diseases*, 23(6):946–956, 2017.

[12] S B Prusiner. Prions. *Proc Natl Acad Sci U S A*, 95:13363–13383, 1998.

[13] J C Abrahantes, M Aerts, et al. Classification of sporadic Creutzfeldt-Jakob disease based on clinical and neuropathological characteristics. *European Journal of Epidemiology*, 22(7):457–465, 2007.

[14] A Ladogana, M Puopolo, E A Croes, et al. Mortality from Creutzfeldt-Jakob disease and related disorders in Europe, Australia, and Canada. *Neurology*, 64(9):1586–1591, 2005.

[15] Piero Parchi and Daniela Saverioni. Molecular pathology, classification, and diagnosis of sporadic human prion disease variants. *Folia Neuropathol.*, 50(1):20–45, 2012.

[16] Ignazio cali, Gianfreanco pouti, Jason smucny, Paul Micharl curtiss, et al. Co-existence of PrPD types 1 and 2 in sporadic Creutzfeldt- Jakob disease of the VV subgroup: phenotypic and prion protein characteristic. *Scientific Reports*, 10(1):1503, 2020.

[17] Pierluigi Gambetti, Qingzhong Kong, Wenquan Zou, Piero Parchi, and G Shu Chen. Sporadic and familial CJD: classification and characterisation. *British medical bulletin*, 66(1):213–239, 2003.

[18] R Wada and W Kucharczyk. Prion infections of the brain. *Neuroimaging Clin N am* , 18(1):183–191, 2008.

[19] Neil Watson, Jean-Philippe, Brandel, Alison Green, Peter Hermann, Anna Ladogana, Terri Lindsay, Janet Mackenzie, Maurizio Pocchiari, Colin Smith, Inga Zerr, and Suvankar Pal. The importance of ongoing surveillance for Creutzfeldt-Jakob disease. *Nature reviews, Neurology*, 17(6):362–379, 2021.

[20] James W. Ironside. Variant Creutzfeldt- Jakob disease: an update. *Folia Neuropathol*, 50(1):50–56, 2012. University of Edinburgh, western general hospital.

[21] Richard Knight. Creutzfeldt-Jakob disease: A rare cause of dementia in elderly persons. *Clin Infect Dis.*, 43(3):340–346, 2006. National Creutzfeldt-Jakob disease surveillance Unit, Edinburgh, United Kingdom.

[22] R Ae et al. Update: Dura mater graft-associated Creutzfeldt-Jakob disease - Japan, 1975-2017. *MMWR Morb. Mortal Wkly Rep.*, 67(9):274–278, 2018.

[23] P Brown, M Preece, J P Brandel, et al. Iatrogenic Creutzfeldt-Jakob disease at the millennium. *Neurology*, 55(8):1075–1081, 2000.

[24] Richard P Conti and Jacqueline M Arnone. Neuropsychiatric symptoms among the major categories of Creutzfeldt-Jakob Disease. *International Journal of Psychiatry in Clinical Practice*, 4(1):1–7, 2016.

[25] L Monari, S C Chen, P Brown, et al. Fatal familial insomnia and familial Creutzfeldt-Jakob disease: different prion proteins determined by DNA polymorphism. *Proc Natl Acad Sci USA*, 91(7):2839–2842, 1994.

[26] H G Wieser, U Schwarz, T Blättler, C Bernoulli, M Sitzler, and K Stoeck. Serial EEG findings in sporadic and iatrogenic Creutzfeldt-Jakob disease. *Clin Neurophysiol*, 115(11):2467–2478, 2004.

[27] I Zerr, W J Schulz-Schaeffer, A Giese, M Bodemer, A Schröter, and K Henkel. Current clinical diagnosis in Creutzfeldt-Jakob disease: identification of uncommon variants. *Ann Neurol*, 48(3):323–329, 2000.

[28] F Caobelli, M Cobelli, C Pizzocaro, M Pavia, S Magnaldi, and U P Guerra. The role of neuroimaging in evaluating patients affected by Creutzfeldt-Jakob disease: a systematic review of the literature. *J Neuroimaging*, 25(1):2–13, 2015.

[29] Aje Green, E J Thompson, and G E Stewart. Use of 14-3-3 and other brain-specific proteins in CSF in the diagnosis of variant Creutzfeldt-Jakob disease. *J Neurol Neurosurg Psychiatry*, 70(6):744–748, 2001.

[30] Marc Manix, Piyush Kalakoti, Miriam Henry, Jai Thakur, Richard Menger, Bharat Guthikonda, and Anil Nanda. Creutzfeldt-Jakob disease: Updated diagnostic criteria, treatment algorithm, and the utility of brain biopsy. *Neurosurg Focus*, 39(5):E2, 2015.

[31] K K Sitammagari and W Masood. Creutzfeldt-Jakob disease. 2020. StatPearls Publishing. Update on March 6, 2021.

[32] D Dormont. how to limit the spread of Creutzfeldt-jakob disease. *Infection control and hospital epidemiology*, 17(8):521–528, 1996.