International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

A Review On: "Creutzfeldt-Jakob Disease"

Swapnanjali S Surwase*[1], Chaitali S Takale[2], Kanchan MJambhale[3]
H.S.B.P.V.T's, GOI, College of Pharmacy, Kashti, Shrigonda, Ahmednagar, Maharashtra, India, 414701.

Submitted: 01-04-2022 Accepted: 09-04-2022

ABSTRACT:
This study covers the validation and context for the establishment of Creutzfeldt-Jakob Disease (CJD) diagnostic criteria, as well as symptoms, pathogenesis, epidemiology, and clinical characteristics, treatment, and future research directions. It is so uncommon, a strong index of suspicion is required not only at the time of diagnosis, but also in the months that follow. The existing diagnostic criteria are insufficient; test sensitivity and specificity vary depending on the disease's genetics and clinical stage. The authors examine CJD, the importance of brain biopsy in this patient, a diagnostic pathway for the patient with fast advancing dementia, and revised diagnostic criteria. There is evidence that thee dementia that may co-occur with CJD is distinct from dementia caused by other neurodegenerative disease. Recent developments in diagnostic procedures have enabled for more reliable case recognition in all forms of CJD, including real-time quaking-induced conversion.

Key Words: Creutzfeldt-Jakob disease(CJD), Ultimate dementia, diagnostic criteria, neurodegenerative disorder.

I. INTRODUCTION:

Creutzfeldt-Jakob disease (CJD) is a rare neurological illness with a fast progression and a 100% fatality rate. There are several types of the disease, with the sporadic kind being the most frequent. This study discusses the reasoning and context for the formation of CJD diagnostic criteria, which include risk factors and neuropathological findings in humans, epidemiology, and clinical characteristics, as well as treatment and future research directions. Future research is needed to better characterize critical symptoms, as well as the manner of therapy transmission efficiency in humans. If a clinician is unsure about all diagnostic testing choices, he or she may perform outdated tests or request a brain biopsy before the diagnostic workup is finished. Despite the fact that the mutant CJD epidemic is definitely on the wane, prevalence data imply that it may be premature to be complacent about public health concerns. In 1922, Spielmeyer coined the term Creutzfeldt-Jakob Disease (CJD) to characterize a disorder described by two German physicians.[1] In 1960, the disease's cardinal feature was identified as the typical clinical picture, electroencephalography (EEG) result, and classic spongiform alterations in the neuropil.[2] There are three types of CJD: familial, sporadic, and acquired. CJD can also be transmitted through iatrogenic causes or by swallowing bovine spongiform encephalopathy-infected beef, resulting in variant CJD.[3] It's a rare case, and it's usually a diagnostic issue for doctors dealing with dementia that's rapidly progressing. It's one of a set of degenerative disorders of the fetal neurological system known as transmissible spongiform encephalopathies, or prion disease, which affects both animals and humans.

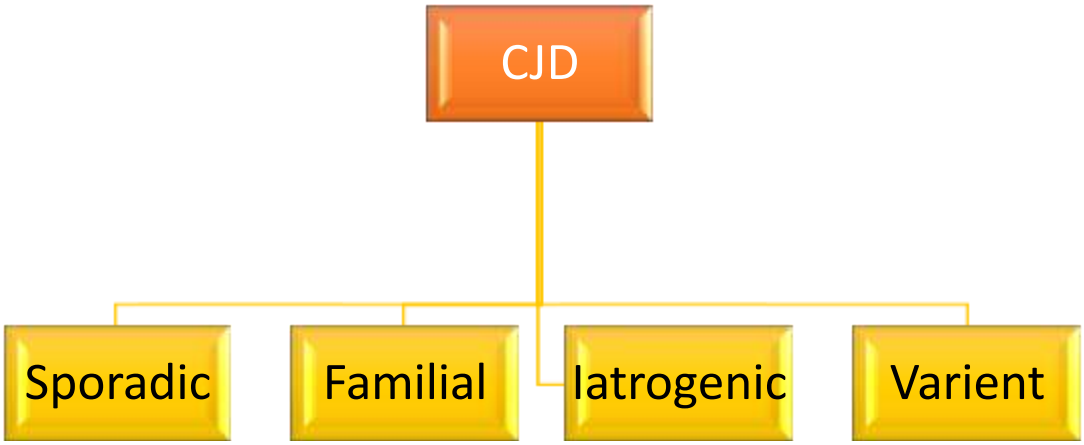
Definition:

What is Creutzfeldt-JakobDisease (CJD)

CJD is a brain wasting illness that is always deadly, marked by symptoms such as memory loss, behavioural changes, and eventually dementia, comparable to Alzheimer's disease.[4] Symptoms usually appear around the age of 60, and 90 % of people die within a year. People with Alzheimer's disease may have memory loss, behavioural abnormalities, lack of coordination, and visual impairments in the early stages of the disease. Mental degeneration becomes more acute as the illness advances, and involuntary movements, blindness, extremity weakness, and coma may ensue[5].

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

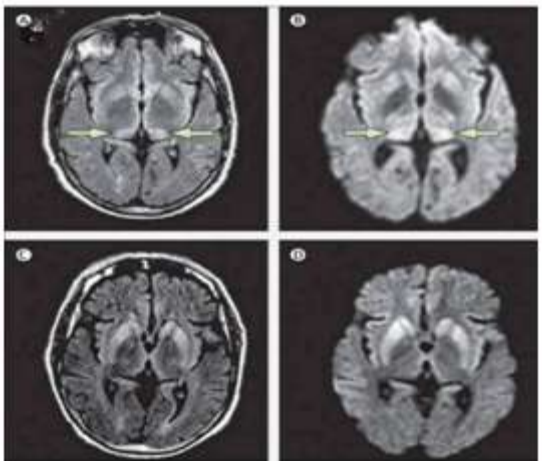
Classification Of Creutzfeldt-Jakob Disease:
CLASSIFICATION OF CJD



1) SPORADIC CJD (sCJD):

Researchers believe it is caused by a spontaneous neurodegenerative sickness, and the theory is that PrPSc is formed as a result of either a somatic mutation in the gene or a random structural alteration in the PrP protein. It is the most common human prion disease, accounting for 85-90 % of cases of CJD. The disease usually appears in the seventh decade of life, and the median time to death is five months, with 90% of patients dying within a year[6] . The genotype at codon 129 of the prion protein gene, which contains a common methionine/valinepolymorphism, produces two forms of protease-resistant prion proteins with different sizes and glycosylation patterns[7].

Diagram:



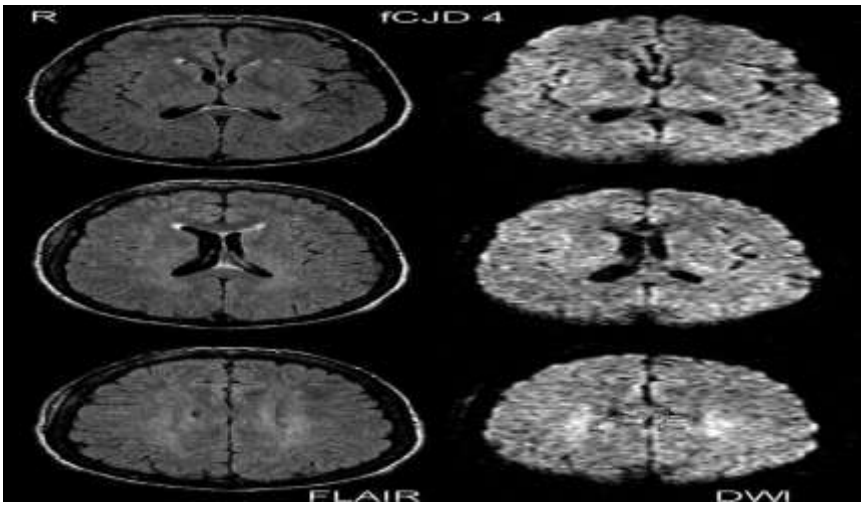
(Fig 1: sporadic CJD)

2) FAMILIAL CJD (fCJD):

Gerstamann-Strausseler-Scheinker (GSS) and fatal familial insomnia (FFI) are well-known variations with identical clinical, radiological, and test findings to sCJD[8]. The familial types of CJD are compared to sporadic and variant CJD. It's a hereditary form of CJD that affects persons who have a family history of the disease and who have a genetic mutation in their prion. Younger persons are more likely to be affected, accounting for 5-15 percent of cases. This mutation increases the likelihood of brain protein converting to the disease-causing version.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

Diagram:

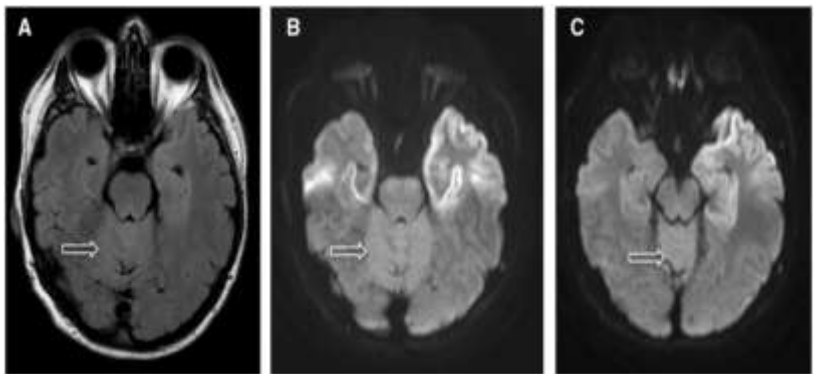


(Fig no: 2 familial CJD)

3) IATROGENIC CJD (iCJD):

In 1974, a patient who underwent a corneal transplant from an infected cadaver was the first case report[9]. More than 60 cases of CJD have been linked to contaminated dura mater transplants, with incubation times ranging from one to fourteen years[10]. During a medical procedure, it is transferred through direct contact with abnormal prion proteins from an external source. CJD has been disseminated in rare cases by reusing contaminated surgical instruments or transplanting particular high-risk tissues from a CJD infected donor. There is no indication that CJD can be spread by casual contact with a patient who has the disease. Contaminated electrodes implanted directly in the brain had a 16–28-month incubation period, whereas peripheral growth hormone injections took anywhere from 5 to 30 years for symptoms to appear[11]. There have been three examples of possible CJD transmission to people who received blood transfusions from a vCJD donor, which is why donors who resided in the United Kingdom (UK) during the BSE pandemic are prohibited [12].

Diagram:



(Fig 3: Iatrogenic CJD)

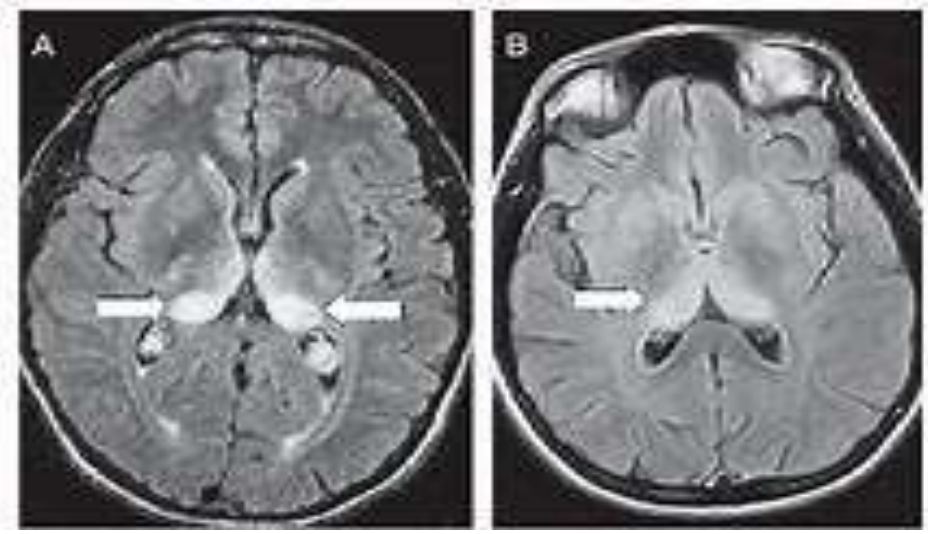
4) VARIENT CJD (vCJD):

Consumption of BSE-infected meat or blood transfusions from vCJD-infected donors has been related to the disease. Variant CJD is a different disease than sporadic or familial CJD, and it is caused by a different prion[7]. The clinical and pathological findings differ from those of other kinds of CJD (Table 1) in that the early course is dominated by psychiatric symptoms before ataxia appears at the 6-month mark. The disease was first discovered in the late 1980s, and its peak incidence was in the early 2000s, giving it an incubation time of 11–12 years According to the initial 1996 study, there have been a total of 229 verified cases

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

globally, the majority of which have been detected in the United Kingdom. There have been four cases in total in the United States, with three of them having previously resided in the United Kingdom UK[13].

Diagram:



(Fig 4: Variant CJD)

Table 1: Finding different types of CJD

CJD Types

Feature	sCJD	vCJD	fCJD	GSS	FFI
Mean age at onset	60-70 yrs	28 yrs	60 yrs	60 yrs	50 yrs
Duration of illness	5 mos	14 mos	6 mos	5 yrs	14 mos
Predominant clinical features	Rapid cognitive decline, myoclonus	Early psychiatric symptoms, then cognitive decline	Similar to sCJD	Cerebellar signs	Insomnia
MRI finding	60%-70% have hypersensitivity in basal ganglia or cortex	Pulvinar signs in 90%	Basal ganglia and cortical hypersensitivity	Rarely abnormal	Non-specific atrophy
EEG finding	PSWCs in 60%-70%	PSWCs negative	PSWCs in 75%	Rarely positive	Rarely positive
14-3-3 status	Positive in 90%	Positive in 50%	Similar in sCJD	Negative	Rarely positive
Genetics	MM1 most common (70%)	MM in 100%	PRNP mutation	P102L is most common mutation	D178N mutation

SYMPTOMS:

1. Creutzfeldt-Jakob disease is characterized by rapid mental decline over a period of months. Typical early indications and symptoms includes:
2. Personality Changes
3. Loss Of Memory
4. Impaired Reasoning
5. Blindness Or Blurred Vision
6. Insomnia
7. Incoordination
8. Difficulty In Speaking And Swallowing

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

9. Jerky Sudden Motions

Pathophysiology:

Even in healthy people and animals, normal cellular prion protein (PrP) is found on cell membranes throughout the body. It has a number of intricate functions that have yet to be fully understood. The prion PrPscrapie (the prion disease of sheep and goats) is produced by the transformation of the normal cellular prion protein PrP into an abnormal, structurally altered, disease-causing form, which subsequently self-propagates and accumulates throughout the brain. Because the results can be positive in Alzheimer's disease or other illnesses that induce neuronal destruction, 14–3-3 detection has little to no relevance in the absence of clinical presentation[20, 21.]

Transmission:

-The majority of cases of Creutzfeldt-Jakob disease are assumed to be caused by prions transmitted through an unknown pathway.

- Creutzfeldt-Jakob disease is caused by a faulty protein that can be inherited (familial form) or transmitted (iatrogenic form) in one of two ways:

*Products containing human growth hormone (hGH).

*Corneal grafting is a procedure that involves the transplantation of corneas.

*Electrode implants or dura grafts.

*HGH extracted from cadaver pituitary glands was used.

*Consumption of an infected animal.

*Cannibalism.

Pathology

Gross pathology:

The brain tissue appears "spongy" on gross histopathological inspection, with areas of perforation inside the brain tissue.

Microscopical pathology:

* CJD is linked to the accumulation of abnormal prion proteins on a microscopic level.

* The microscopic findings listed below may be present in CJD:

* The presence of florid plaques, which are spherical, tightly packed deposits of aberrant prion protein (in variant CJD).

*Spongiform alterations.

*Neuronal degeneration.

* The presence of prion protein in the brain[14].

Diagnosis:

The tests will be performed by a neurologist (a doctor who specializes in nervous system problems) to rule out other conditions that have similar symptoms, such as Alzheimer's disease, Parkinson's disease, or a brain tumor. The only way to confirm a CJD diagnosis is to perform a brain biopsy or, more usually, a post-mortem study of the brain. When making a diagnosis, specialists from the National CJD Research and Surveillance Unit in Edinburgh and the National Prion Clinic in London advise local teams.Given this diagnostic conundrum, MRI of the brain is becoming a more important tool in the examination of patients suspected of having CJD. Most significantly, an MRI can rule out alternative, potentially curable causes of encephalopathy. In some cases of spontaneous Creutzfeldt-Jakob disease, Western blot and immunohistochemistry were used to investigate the biochemical properties and intracerebral distribution of protease-resistant prion protein[15].

- **Clinical And Pathological Characteristics Distinguishing Classic And Varient Cjd[16]**

Characteristics	Classic CJD	Variant CJD
Presence of "Florid Plaque" on neuropathology	Rare or absent	Present in large number
Immunohistochemical analysis of brain tissue	Variable accumulation	Marketed accumulation of protease-resistance prion protein
Presence of agent in lymphoid tissue	Not readily detected	Readily detected
Increased glycoform ratio on immunoblot analysis of protease-resistance prion protein	Not reported	Marked accumulation of protease-resistance prion protein

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

***Source:**

Variant Creutzfeldt-Jakob Disease and Bovine Spongiform Encephalopathy, by E. Belay and L. Schonberger. 849-862 in Clin Lab Med, 2002.

• On brain magnetic resonance imaging (MRI), an aberrant signal in the posterior thalami on T2 and diffusion-weighted images, as well as a fluid-attenuated inversion recovery sequence; in the right clinical setting, this signal is highly specific for vCJD.

Treatment:

Currently, treatment consists on attempting to keep the patient as comfortable as possible while also lowering symptoms with medications. Sedatives and antidepressants, for example, can be used to treat psychological symptoms of CJD like anxiety and depression, and drugs like clonazepam and sodium valproate can be used to treat muscle jerks and tremors.

Specialist team:

When someone is suspected of having CJD, they are sent to the National Care Team for CJD at the National CJD Research and Surveillance Unit in Edinburgh or the National Prion Clinic in London for diagnosis and treatment. Local services, such as the person's GP, social worker, physiotherapist, and occupational therapist, will be contacted by a doctor and nurse from these agencies. Specialist teams work alongside the local care team to provide diagnostic and clinical and emotional support to patients and their families. Doctors and nurses, occupational therapists, nutritionists, continence experts, and social workers may all be part of a local care team.

Potential treatments for Creutzfeldt-Jakob Disease (CJD):

Creutzfeldt-Jakob disease and other human prion illnesses are always fatal, and the underlying process has yet to be identified. However, there are a number of potential treatments in the works or being considered. It is important to note that no medication has been found to definitively reduce or stop the disease process in individuals with any form of CJD to date. Quinacrine and PentosanPolysulphate, as well as Flupirtine[16], have received media attention as prospective treatments. Quinacrine is now being studied in a PRION-1 trial financed by the Medical Research Council.

Quinacrine:

'Acridine and phenothiazine derivatives as prion disease pharmacotherapeutics' (Korth et al.). This study found that a number of drugs inhibited the development of the disease-associated type of prion protein in scrapie-infected neuroblastoma cells, with quinacrine and chlorpromazine being the most effective.

PentosanPolysulphate:

PentosanPolysulphate (PPS) is an anti-thrombotic and anti-inflammatory compound produced from beechwood. It has been utilised in the treatment of thrombotic diseases and interstitial cystitis in standard clinical practise for some time.

Preventive measures:

Normal sterilisation methods like cooking, washing, and boiling do not destroy prions.

When working with a person who has CJD, caregivers, health care workers, and undertakers should take the following precautions:

* Before eating, drinking, or smoking, wash your hands and any exposed skin.
* Apply waterproof dressings to cuts and abrasions.
* When touching a patient's tissues and fluids, or dressing the patient's wounds, use surgical gloves.
* Do not cut or stick themselves with equipment contaminated with blood or other tissue from the patient[18].
* Soak instruments that have come into contact with the patient for an hour or longer in undiluted chlorine bleach, then sterilize them in distilled water for at least one hour at 132 - 134 degrees Centigrade in an autoclave (pressure cooker) [19].

*In the UK and other countries, continuing surveillance of both BSE and CJD is essential to ensure that the scope of this risk is effectively monitored and that all practicable measures are taken to prevent further human exposure to the BSE agent[19].

II. CONCLUSION:

To summarize, sCJD is a deadly, progressive, and incurable neurodegenerative disease that can first masquerade as other significant neurologic disorders. Because it is so uncommon, a strong index of suspicion is required not only at the time of diagnosis, but also in the months that follow. Creutzfeldt-Jakob disease is a deadly neurological disorder that frequently founds by doctors. Given its rarity, published diagnostic criteria can help with diagnosis, but they're out of date and don't take into account modern research laboratory procedures.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 841-847 www.ijprajournal.com ISSN: 2456-4494

REFERENCE:

[1]. Spielmeyer W: Die histopathologischeForschung in der Psychiatrie. KlinWochenschr 1:1817–1819, 1922.
[2]. Nevin S, McMenemey WH, Behrman S, Jones DP: Subacute spongiform encephalopathy—a subacute form of encephalopathy attributable to vascular dysfunction (spongiform cerebral atrophy). Brain 83:519–564, 1960.
[3]. Knight RS, Will RG: Prion diseases. J NeurolNeurosurg Psychiatry 75 (Suppl 1): i36–i42, 2004
[4]. The Encyclopedia of Alzheimer's Disease-Google Book-pg.71-72.
[5]. "Creutzfeldt-Jakob Disease Fact Sheet," NINDS. (National Institute of Neurological 6. Disorders and Stroke) Publication date March 2003.
[6]. Johnson RT, Gibbs CJ Jr: Creutzfeldt-Jakob disease and related transmissible spongiform encephalopathies. N Engl J Med 339:1994–2004, 1998.
[7]. Creutzfeldt-Jakob disease, General Fact Sheethttp://www.michigan.gov/documents/mdch/GeneralCJDFact_300086_7.pdf.
[8]. Mead S: Prion disease genetics. Eur J Hum Genet 14:273–281, 2006.
[9]. Duffy P, Wolf J, Collins G, DeVoe AG, Streeten B, Cowen D: Possible person-to-personTransmission of Creutzfeldt-Jakob disease. N Engl J Med 290:692–693, 1974 (Letter).
[10]. Centers for Disease Control and Prevention: CreutzfeldtJakob disease associated with cadaveric dura mater grafts -- Japan, January 1979-May 1996. MMWR Morb Mortal Wkly Rep 46:1066–1069, 1997.
[11]. United States Public Health Service: Public Health Service Interagency Coordinating Committee Report on Human Growth Hormone and CJD. Washington, DC: US Public Health Service, 1997, Vol 14, pp 1–11.
[12]. Llewelyn CA, Hewitt PE, Knight RS, Amar K, Cousens S, Mackenzie J, et al: Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. Lancet363:417–421, 2004.
[13]. Maheshwari A, Fischer M, Gambetti P, Parker A, Ram A, Soto C, et al: Recent US Case of Variant Creutzfeldt-Jakob Disease-Global Implications. Emerg Infect Dis 21:750–759,2015.
[14]. Sellars, RJ.; Collie, DA.; Will, RJ. (2002). "Progress in understanding Creutzfeldt-Jakobdisease". AJNR Am J Neuroradiol. 23 (7): 1070–2. PMID 12169459.
[15]. Parchi P, Castellani R, Capellari S, Ghetti B, Young K, Chen SG, Farlow M, Dickson DW, Sima AA, Trojanowski JQ, Petersen RB, Gambetti P.Molecular basis of phenotypic variability in sporadic Creutzfeldt-Jakob disease. Ann Neurol. 1996 Jun;39(6):767-78.
[16]. Centers for Disease Control and Prevention. Date: December 13, 2010
[17]. Potential treatments for Creutzfeldt-Jakob Disease (CJD). Aug 08,2004.www.medicalnewstoday.com
[18]. Creutzfeldt-Jakob Disease index, July1, 2012.Mednet.com
[19]. Zeidler M, Ironside JW. The new variant of Creutzfeldt-Jakob disease. Rev Sci Tech. 2000 Apr;19(1):98-120.Department of Clinical Neurology, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, United Kingdom.
[20]. Brown P, Brunk C, Budka H, Cervenakova L, Collie D, Green A, et al: WHO Manual for Surveillance of Human Transmissible Spongiform Encephalopathies, including Variant Creutzfeldt-Jakob Disease. Geneva: World Health Organization, Communicable Disease Surveillance and Response, 2003.
[21]. Brown P, Preece M, Brandel JP, Sato T, McShane L, Zerr I, et al: Iatrogenic Creutzfeldt-Jakob disease at the millennium. Neurology 55:1075–1081, 2000.