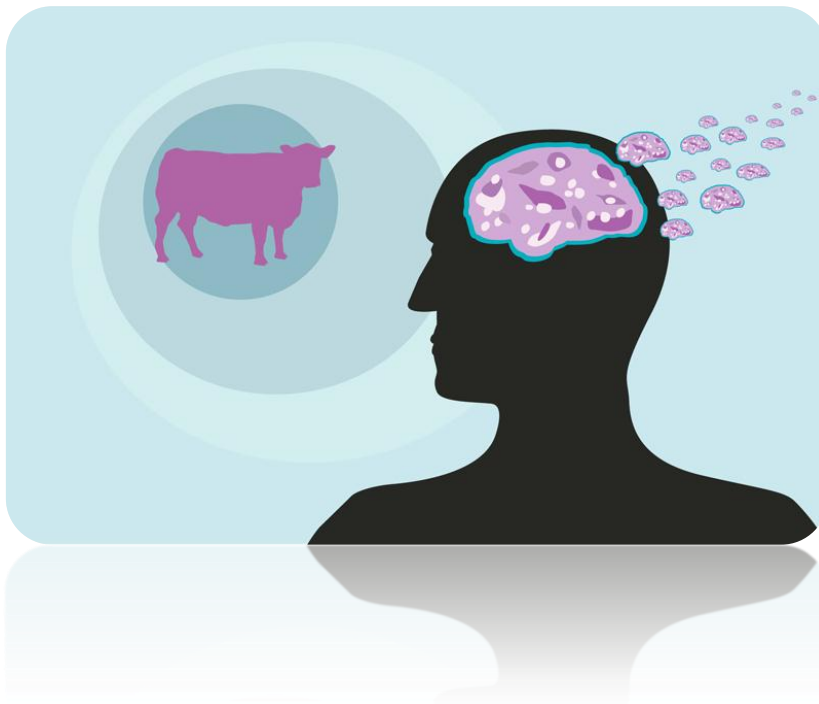




وزارة التعليم العالي
جامعة الملك سعود
كلية العلوم
قسم الأحياء الدقيقة

MEDICAL VIROLOGY

Variant creutzfeldt-jacob disease



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1. Topic. (variant creutzfeldt – Jacob disease)

2. Introduction:

2.1 History of Mad Cow Disease In Humans :

Mad cow disease is a fatal disease that slowly destroys the brain and spinal cord (central nervous system) in cattle. It also is known as bovine spongiform encephalopathy, or BSE.

People cannot get mad cow disease. But in rare cases they may get a human form of mad cow disease called variant Creutzfeldt–Jakob disease (vCJD), which is fatal.

This can happen if you eat nerve tissue (the brain and spinal cord) of cattle that were infected with mad cow disease. Over time, vCJD destroys the brain and spinal cord.

There is no evidence that people can get mad cow disease or vCJD from eating muscle meat—which is used for ground beef, roasts, and steaks—or from consuming milk or milk products.

The first case of vCJD was reported in 1996. Since then, there have been a few cases of vCJD reported in the world. Most of the cases have been in countries that are part of the United Kingdom (England, Scotland, Wales, and Northern Ireland).

In December 2003, mad cow disease was discovered in one cow in the United States. Before this cow was found to have the disease, the cow was slaughtered and its muscle meat was sent to be sold in grocery stores. But its organs and nerve tissue were not used for human food. Although mad cow disease cannot be spread through muscle meat, the United States Department of Agriculture (USDA) quickly traced the meat and removed it from grocery stores.

Since 2004, only three more cows in the United States have been found to have mad cow disease. The most recent case of BSE was found in April 2012 in a cow in California. {1} [\(Reem\)](#)

2.2 Introduction of the virus..

It's called mad cow disease because it affects a cow's nervous system, causing a cow to act strangely and lose control of its ability to do normal things, such as walk. An infected cow would act "mad," which sometimes means mentally ill. It's also called bovine spongiform encephalopathy (BSE){2}, It's related to a disease in humans called variant Creutzfeldt–Jakob disease (vCJD) .Both disorders are universally fatal brain diseases caused by a prion. This is a protein particle that lacks DNA (nucleic acid). It's believed to be the cause of various infectious diseases of the nervous system. Eating infected cattle products, including beef, can cause a human to develop mad cow disease. Creutzfeldt–Jakob Disease (CJD) is a rare, fatal brain disorder that causes a rapid, progressive dementia (deterioration of mental functions), as well as associated neuromuscular disturbances. The disease, which in some ways resembles mad cow disease, traditionally has affected men and women between the ages of 50 and 75. The variant form, however,

affects people (the median age of onset is 28) and has observed features that are not typical as compared with CJD. Mad cow disease is a progressive, fatal neurological disorder of cattle resulting from infection by a prion. It appears to be caused by contaminated feed that contains the prion agent.{3} (somaya)

2.3 The distribution of this disease..

The extraordinary commercial and public-health consequences of BSE, as well as the near-global distribution of products derived from cattle, have generated a considerable amount of attention from industry, government and the general public. As a result, there is a daunting volume of information—not all of it reliable—surrounding the nature of mad-cow disease {4} M disease first identified in 1986 in the United Kingdom by disease endemic in sheep for more than 200 years, the disease spread epidemic in English cattle epidemic peak was between 1992–1993, but with disease control measures the disease began to recede as the disease epidemic appeared also in Northern Ireland. Then the disease in cows imported from the United Kingdom in Ireland, Oman, Germany, Denmark, Italy appeared as the disease in cows imported as well as local in many European countries such as France, Portugal, Switzerland, the Republic of Ireland, Germany, Denmark, outside Europe such as the Falkland Islands and Canada. Undiagnosed illness in Egypt and it's worth mentioning that Egypt is not implemented by any of the programs recommended by CDC's Office in Paris to monitor the disease. {5}

Pathogen: infectious agent transferable pathogen o move known as prion protein is a type of axle-free nucleic acids and does not affect it influences that cause hydrolysis of nucleic acids is similar with the causative and it is not known whether the contagion factor that causes mad cow disease is the same causative of sheep and cattle to befall mutated or independent, the causative agent of mad cow disease does not cause any immune reaction because the youngster the finite and therefore there is no way to detect in animal. {6} The working features as resistant to environmental effects and is not affected by the most effective means of sterilization with viruses is resistant to boiling and freezing highway as unaffected by 20% formalin solution and resist heat, temperatures are used during cooking does not kill him or even those used in sterilization. It is not affected by ultraviolet light, and found that he retains his ability to infection in brain tissue buried in the soil for three years but unaffected by steam sterilization with chlorine solution 2% and 4% sodium hydroxide solution.{7} (noura,joud)

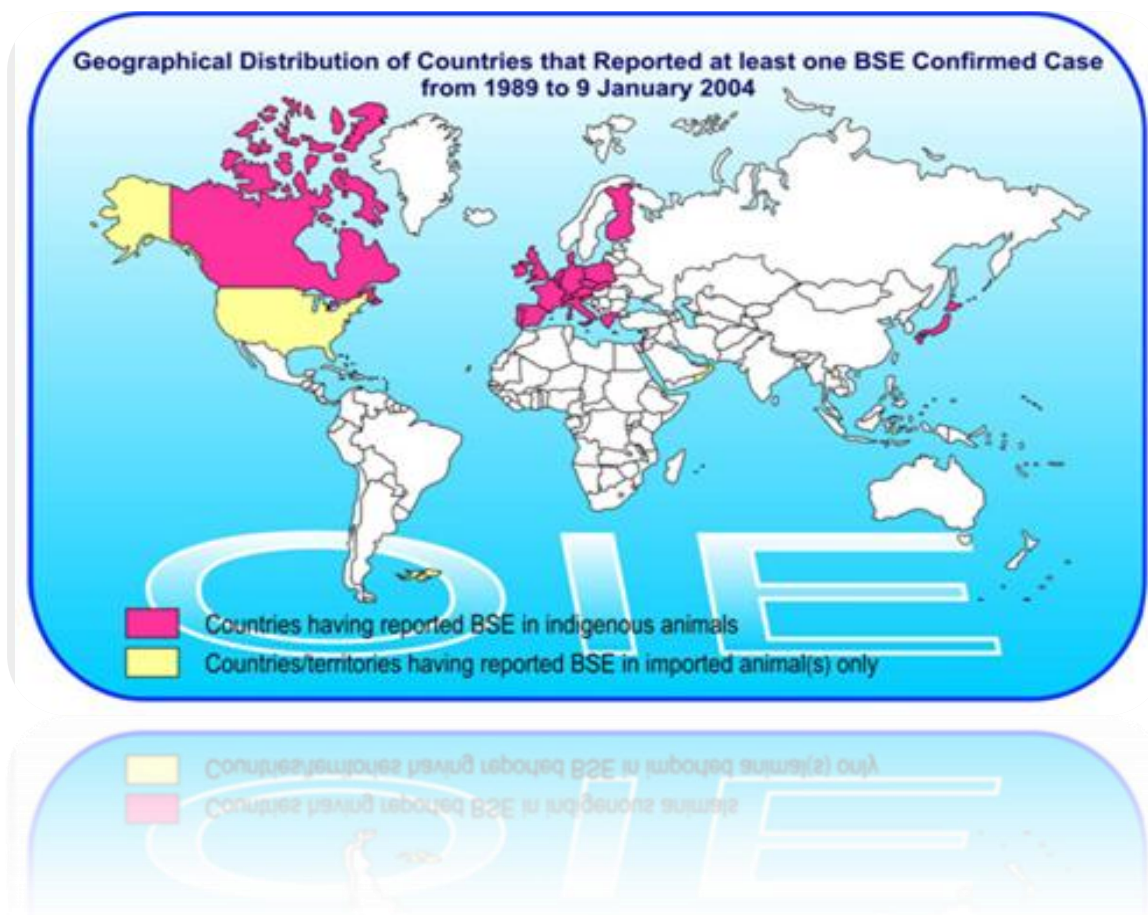
2.4 Epidemic..

It seemed that these diseases due to uncharacteristic patients reasoned by none of the isolation and the Prion protein, what is this: a nurse working no bacterial and viral was veterinarians were the first to care for him. Because of its spread from human being to another because the cow food switch based on human being, resulting in encephalopathy when protected from cows before.{8}

These diseases (mad cow) common properties are all a sponge-form encephalopathy brain evolution is too slow, and practical diagnosis by Postmortem ensure quality and infection. {9}

This assumption is based on the fact that these ten injuries that killed eight patients, was characterized by occur when persons are not eligible for sickness "Jacob," and the fact that the lesions caused by this disease in the human brain, somewhat resemble the lesions caused by mad cow disease.{10}

(Hajar)



3. Classification of the virus: {11}

Order	As infectious, contagious, or zoonotic,
Family	<p>Variant (vCJD) This is thought to be caused by the consumption of food contaminated with prions, which also cause BSE.</p> <p>Sporadic (sCJD) This accounts for 85% of cases of CJD.</p> <p>Familial (fCJD) This accounts for the majority of the other 15% cases of CJD.</p>
Gene	<p>Gene symbol CJD For the prion protein (PRNP)</p>

(Joud)

4. Structure and genome:

- The envelope is a phospholipid bilayer membrane that was obtained from the cell in which the virus arose

4.1 Size:

- Hantaviruses have 3 genes that encode 4 polypeptides
- Pox viruses have nearly 200 genes

4.2 nveloped or not:

- Some viruses have an envelope

4.3 Nucleic acid:

- Such an infectious agent would have to contain a very short segment of nucleic acid. {12}

(Hajar)

5. Proteins (Virulence Factors):

Prions :

A communicable go-between exclusively complete of protein and called it prion [preen-on], small for "proteinaceous communicable" atom. its discovery that Creutzfeldt–Jakob disease (CJD) was caused by prions.

The usual prion protein is originated through the body and intelligence. While not vital to lifetime, it fixes appear to production a role in serving your neurons connect and conveyance reserves. Its amino acid chains crinkle into a mostly helical form.

How do prions cause CJD?

In Creutzfeldt–Jakob disease and other prion diseases, the prion protein folds into an strange shape where the flat expanse organization replaces the helix, which incomes the protein can't do its normal job.

Different any other celebrated protein, abnormal prion proteins are infectious. This was a fundamental detection since proteins don't comprise the hereditary physical that permits diseases and microorganisms to replicate.

These misfiled proteins persuade other prions to misfile. Then these misfiled prions erect up in the intelligence and cause the septic brain cells to die. Once the infected compartments die, prions are unconfined into usual matter and go on to contaminate other cells deprived of any response from the absolved organism. Finally, large collections of cells die foremost to the psychological and communicative indications of prion maladies.

Prion maladies are the only recognized illnesses that can be irregular, hereditary or infective.

Protein is mainly used to shape, preserve and overhaul body matters, but there are thousands of different proteins that carry out a diversity of jobs in your figure. The structure of a protein regulates its function.

Loose threads of amino acid are the "structure wedges" of proteins. These threads then fold and twist into multifaceted three–D forms that permit the protein to do its job. Two mutual forms are an important coil (looks like a spiral staircase) and a beta piece (a flattened out shape).

The protein that prions are made of (PrP) is found throughout the body, even in healthy people and animals.

However, PrP found in infectious material has a different structure and is resistant to proteases, the enzymes in the body that can normally break down proteins PrPC is a normal protein found on the membranes of cells. It has 209 amino acids (in humans), one disulfide bond, a molecular mass of 35–36 kDa and a mainly alpha–helical structure. 'Prion' is a term first used to describe the mysterious infectious agent responsible for several neurodegenerative diseases found in mammals, including Creutzfeldt–Jakob

disease (CJD) in humans. {13}

(Noura)

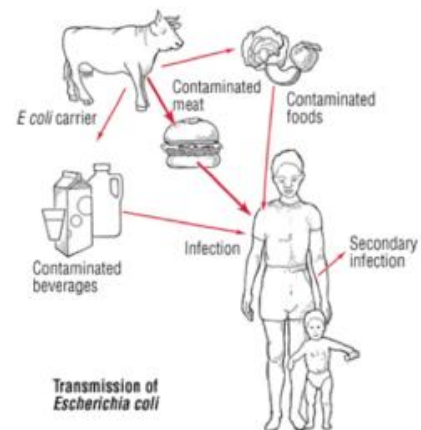
6. Transmission.

For vCJD, the exact route of transmission from BSE to humans is uncertain, but is likely to be linked to contaminated foods of bovine origin. Probable secondary transmission of vCJD via blood transfusion has been reported. Incubation not known precisely, likely to be long.

Mode of transmission for sCJD is not known; de novo spontaneous generation of self-replicating protein has been hypothesized. No clear evidence of risk from diet, previous surgery, blood transfusion, occupational or animal exposure, the possibility that sporadic CJD arises through other unrecognized environmental exposure cannot be dismissed.

Familial CJD (fCJD) is an inherited condition and cases represent 20% to 15% of the total number of CJD cases. Gerstmann-Sträussler-Scheinker disease (GSS) and fatal familial insomnia (FFI) are very rare forms of fCJD.

Iatrogenic CJD infection is inadvertently transmitted usually from a case with sCJD in the course of medical/surgical treatment, e.g. human pituitary hormone therapy, human dura mater grafts, corneal grafts or neurological instruments. {14}



(somaya)

7. Penetration and the Target Organ.

These include the public wellbeing subjects that mark family memberships of a enduring with hereditary prion illness, exactly their limit from plasma and organ part. Informed agreement should be procured and annals kept intimate. Persons with a optimistic test consequence essential preparations for lasting follow-up and valuations. {15}

(Noura)

8. Replication Cycle (the main site).

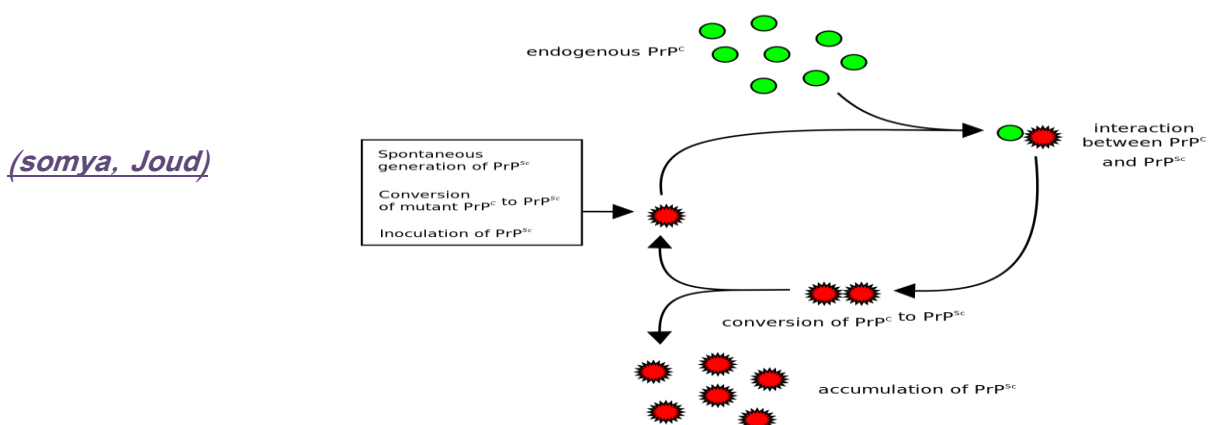
Prions (the name is derived from proteinacious infectious particle) is the name used by many scientists to describe the pathogen that causes transmissible spongiform encephalopathies (TSE) which are neurodegenerative diseases in mammals. Prions are a disease-causing form of a normal protein called cellular prion protein (PrP^C) that is located primarily on the surface of central nervous system cells but also in other tissues of the body in mammals. The specific function of the normal prion protein (PrP^C) is not clearly understood, but in experimental models it appears to play a role in protecting cells and helping them respond to oxygen deficiency.

Prions are extremely small, smaller than viruses, and even through an electron microscope only aggregations (clusters), not individual prions, can be seen.

Prions are unique pathogens in that they appear to have no nucleic acid and thereby differ from viruses, bacteria, fungi and other pathogens. Prions are resistant to procedures that break down nucleic acid and destroy biological forms of pathogens.

In addition, prions differ from other pathogens in that they are responsible for genetic, sporadic and acquired forms of neurodegenerative disease. Also, because prions are an abnormal form of a normal protein that is genetically encoded, they do not produce an immune response in the host as would a foreign infectious agent.

Lacking nucleic acid, prions cannot reproduce, but they replicate by stimulating normal cellular prion protein to refold into a form called PrP^{Sc} – named after scrapie, the first TSE discovered. The conversion of normal prion protein (PrP^C) into abnormal prion protein (PrP^{Sc}) and replication of prions in the brain causes degeneration of neural tissue and, ultimately, death. The process by which the prion recruits normal prion protein (PrP^C) to convert to the disease-causing form remains unknown. {16}



9. Assembly and Egression.

NO assembly and egression

10. What are the symptoms of vCJD?

Variant Creutzfeldt–Jakob disease (vCJD) causes the brain to become damaged over time. It is fatal.

Symptoms include:

- *Tingling, burning, or prickling in the face, hands, feet, and legs. But there are much more common illnesses that cause these same symptoms. Having tingling in parts of your body does not mean you have vCJD.*
- *Dementia.*
- *Psychotic behavior.*
- *Problems moving parts of the body. As the disease gets worse, a person is no longer able to walk.*
- *Coma.*

If a person does eat nerve tissue from an infected cow, he or she may not feel sick right away. The time it takes for symptoms to occur after you're exposed to the disease is not known for sure, but experts think it is years. {17}

(Reem)

11. Diagnosis and Cytopathic effect.

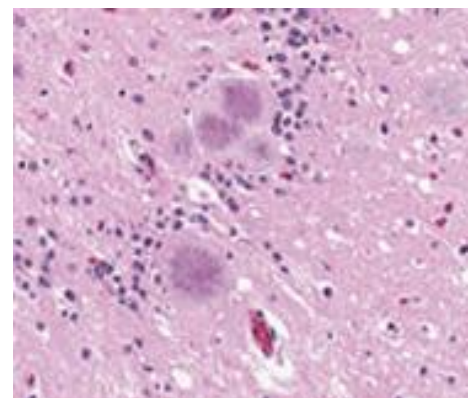
A diagnosis of Creutzfeldt–Jakob disease (CJD) is usually based on medical history, symptoms and a series of tests.

A neurologist (a doctor who specialises in conditions of the nervous system) will carry out the tests to rule out other conditions with similar symptoms, such as Alzheimer's disease, Parkinson's disease or a brain tumour.

The only way to confirm a diagnosis of CJD is to examine the brain tissue by carrying out a brain biopsy, or more commonly (after death) by post–mortem examination of the brain.

During a brain biopsy, a surgeon drills a tiny hole into the skull and removes a small piece of brain tissue using a very thin needle. It's carried out under general anaesthetic, which means the person will be unconscious during the procedure. {18}

This slide shows sponge–like lesions in the brain tissue of a CJD patient. (Image courtesy Ermias Belay){19}



Rapid symptom progression is one of the most important clues that a person may have Creutzfeldt–Jakob disease.

A clinical neurologist will rule out other conditions with similar symptoms and check for some common signs of CJD by carrying out the tests below:{20}

There is no single test — or any combination of tests — that can conclusively diagnose sporadic CJD in a living person, but the following tests may help determine whether an individual has CJD:

Electroencephalogram (EEG) measures the brain's patterns of electrical activity similar to the way an electrocardiogram (ECG) measures the heart's electrical activity.

Brain magnetic resonance imaging (MRI) can detect certain brain changes consistent with CJD.

Lumbar puncture (spinal tap) tests spinal fluid for the presence of certain proteins.{21} (somaya)

12. Control the virus and Prevention.

Concealment cuts and scrapes with water-resistant dressings. Wear surgical gloves when treatment a patient's matters and fluids or bandage the patient's injuries. Avoid wounding or sticking themselves with gadgets contaminated by the patient's blood or other materials. Use disposable bedcovers and other cloth for contact with the patient. If throwaway resources are not available, even cloth should be saturated in straight chlorine lighten for an hour or more, and then eroded 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 tools that have come in interaction with the patient in straight chlorine lighten for an hour or more, and then use an autoclave (pressure cooker) to neuter them in purified aquatic for at least one period at 132 – 134 gradations Centigrade.{22} (Hajar)

13. How is vCJD treated?

There is no cure for vCJD. Treatment includes managing the symptoms that occur as the disease gets worse.{23} (Reem)

14. Host Immune Defense.

The nonappearance of a host immune response in prion disease allows immunotherapeutic methods to be used, and the effectiveness of antibody action has lately been established in both compartment philosophy and physical replicas of prion illness. {24}

(Noura)

15. Genetic(Gene Mutation):

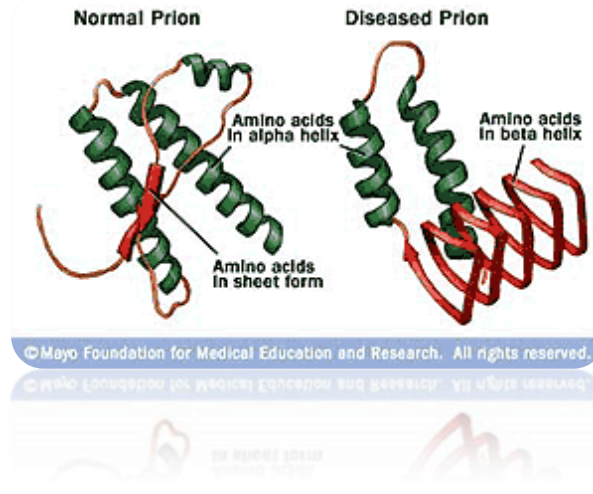
Unknown

16. Recent discoveries.

1996 Summary Background Epidemiological surveillance of Creutzfeldt–Jakob disease (CJD) was reinstated in the UK in 1990 to identify any changes in the occurrence of this disease after the epidemic of bovine spongiform encephalopathy (BSE) in cattle.

Methods Case ascertainment of CJD was mostly by direct referral from neurologists and neuropathologists. Death certificates on which CJD was mentioned were also obtained. Clinical details were obtained for all referred cases, and information on potential risk factors for CJD was obtained by a standard questionnaire administered to patients' relatives. Neuropathological examination was carried out on approximately 70% of suspect cases. Epidemiological studies of CJD using similar methodology to the UK study have been carried out in France, Germany, Italy, and the Netherlands between 1993 and 1995.

Findings Ten cases of CJD have been identified in the UK in recent months with a new neuropathological profile. Other consistent features that are unusual include the young age of the cases, clinical findings, and the absence of the electroencephalogram features typical for CJD. Similar cases have not been identified in other countries in the European surveillance system.



Interpretation These cases appear to represent a new variant of CJD, which may be unique to the UK. This raises the possibility that they are causally linked to BSE. Although this may be the most plausible explanation for this cluster of cases, a link with BSE cannot be confirmed on the basis of this evidence alone. It is essential to obtain further information on the current and past clinical and neuropathological profiles of CJD in the UK and elsewhere.{25}

Several molecular subtypes of sporadic Creutzfeldt–Jakob disease have been identified and electroencephalogram and cerebrospinal fluid biomarkers have been reported to support clinical diagnosis but with variable utility according to subtype. In recent years, a series of 2009 Publications have demonstrated a potentially important role for magnetic resonance imaging in the pre–mortem diagnosis of sporadic Creutzfeldt–Jakob disease. Magnetic resonance imaging signal alterations correlate with distinct sporadic Creutzfeldt–Jakob disease molecular subtypes and thus might contribute to the earlier identification of the whole spectrum of sporadic Creutzfeldt–Jakob disease cases. This multi–centre international study aimed to provide a rationale for the amendment of the clinical diagnostic criteria for sporadic Creutzfeldt–Jakob disease. Patients with sporadic Creutzfeldt–Jakob disease and fluid attenuated inversion recovery or diffusion–weight imaging were recruited from 12 countries. Patients referred as ‘suspected sporadic Creutzfeldt–Jakob disease’ but with an alternative diagnosis after thorough follow up, were analysed as controls. All magnetic resonance imaging scans were assessed for signal changes according to a standard protocol encompassing seven cortical regions, basal ganglia, thalamus and cerebellum. Magnetic resonance imaging scans were evaluated in 436 sporadic Creutzfeldt–Jakob disease patients and 141 controls. The pattern of high signal intensity with the best sensitivity and specificity in the differential diagnosis of sporadic Creutzfeldt–Jakob disease was identified. The optimum diagnostic accuracy in the differential diagnosis of rapid progressive dementia was obtained when either at least two cortical regions (temporal, parietal or occipital) or both caudate nucleus and putamen displayed a high signal in fluid attenuated inversion recovery or diffusion–weight imaging magnetic resonance imaging. Based on our analyses, magnetic resonance imaging was positive in 83% of cases. In all definite cases, the amended criteria would cover the vast majority of suspected cases, being positive in 98%. Cerebral cortical signal increase and high signal in

caudate nucleus and putamen on fluid attenuated inversion recovery or diffusion-weight imaging magnetic resonance imaging are useful in the diagnosis of sporadic Creutzfeldt–Jakob disease. We propose an amendment to the clinical diagnostic criteria for sporadic Creutzfeldt–Jakob disease to include findings from magnetic resonance imaging scans.{26}

Currently, the diagnosis of vCJD can only be confirmed following pathological examination of the brain post mortem. Characteristically, multiple microscopic and abnormal aggregates encircled by holes are seen in the brain tissue, resulting in a daisy-like appearance described by the term "florid plaques".{27}

(Somaya)



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