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MEDICAL SCIENCE

UNIT 1: Human Health and Disease

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Level 3 Diploma in Medical Science

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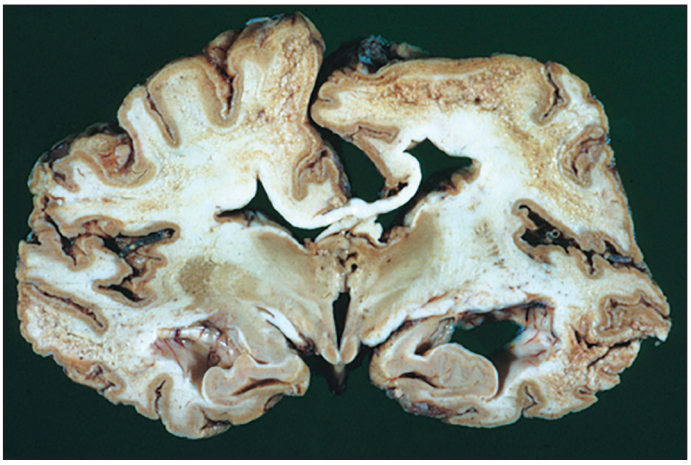
Estimate doubled for variant CJD carriers in UK

adapted from an article from www.bbc.co.uk/news/health-24525584….

Creutzfeldt-Jakob disease (CJD) is a fatal brain condition.



Researchers believe one in 2000 people in the UK is a carrier of the disease linked to eating contaminated beef.
Their estimate comes from studying more than 32000 samples of human tissue removed during appendix operations carried out between 2000 and 2012 at 41 hospitals.
It remains unclear if any of these carriers will ever develop symptoms. To date, there have been 177 UK deaths from variant CJD (vCJD). Most of these occurred in the late 1990s and early 2000s.

Will these people develop disease and can they transmit it?

It appears that relatively few people who catch the infectious agent develop symptoms. People can be “silent” carriers for decades and not even know it.

The research identified 16 such carriers out of the thousands of appendix tissue samples studied.

The link between vCJD and bovine spongiform encephalopathy (BSE), known as mad cow disease, was discovered in 1996. There have since been strict controls to prevent meat from infected cattle entering the food chain.

However, the average time it takes for the symptoms of vCJD to occur after initial infection is still unclear. This means people exposed to infected meat before the food controls were introduced continue to develop vCJD, and may spread it to others.

Experience tells us that the disease could be transmitted from human to human via blood. In the UK, there have been four reported cases of vCJD associated with a blood transfusion. Blood donor services take measures to ensure blood is not infected but there is no test to screen for vCJD, although scientists are working on this. And there is currently no cure for the disease.

Scientists at University College London, who led the research, said: “We do not know what will happen. Will these people develop disease and can they transmit it? There are many questions we still do not know the answers to.”

Researchers, at the MRC Prion Unit at UCL Institute of Neurology, said: “Given the high levels of infection indicated by this research, it is now crucial we establish how many people in the UK harbour that infection in their bloodstream in order to adequately assess the risks of transmission through contaminated blood donations.”

Creutzfeldt-Jakob disease (CJD)

Creutzfeldt-Jakob disease (CJD) is a rare, fatal condition that affects the brain. It causes brain damage that worsens rapidly over time.

What causes CJD?

CJD is caused by an abnormal, infectious protein called a prion. Normal, harmless, prion proteins are found in almost all body tissues, but are at their highest levels in brain and nerve cells. Their role is unknown but it is thought that they may be involved in transporting messages between certain brain cells.

When there is a mistake in the production of the prion protein it leads to these abnormal prions. These abnormal prions will collect in high levels in the brain and will cause irreversible damage to the nerve cells, resulting in a number of the symptoms being experienced by the infected person.

These prions are infectious, but they cannot be destroyed by high temperatures and unlike bacteria and viruses they are not killed by radiation, antibiotics or antiviral medicines. They can also survive in nerve tissue for a long time after death.

How do prions cause CJD?

The abnormal prions that accumulate in the brain cause other prion proteins to change. This causes the brain cells to die, releasing more prions to infect other brain cells. This infection causes small holes to develop in the brain, giving a sponge-like appearance. It is this damage to the brain that causes mental and physical impairment which is associated with CJD which eventually leads to death.

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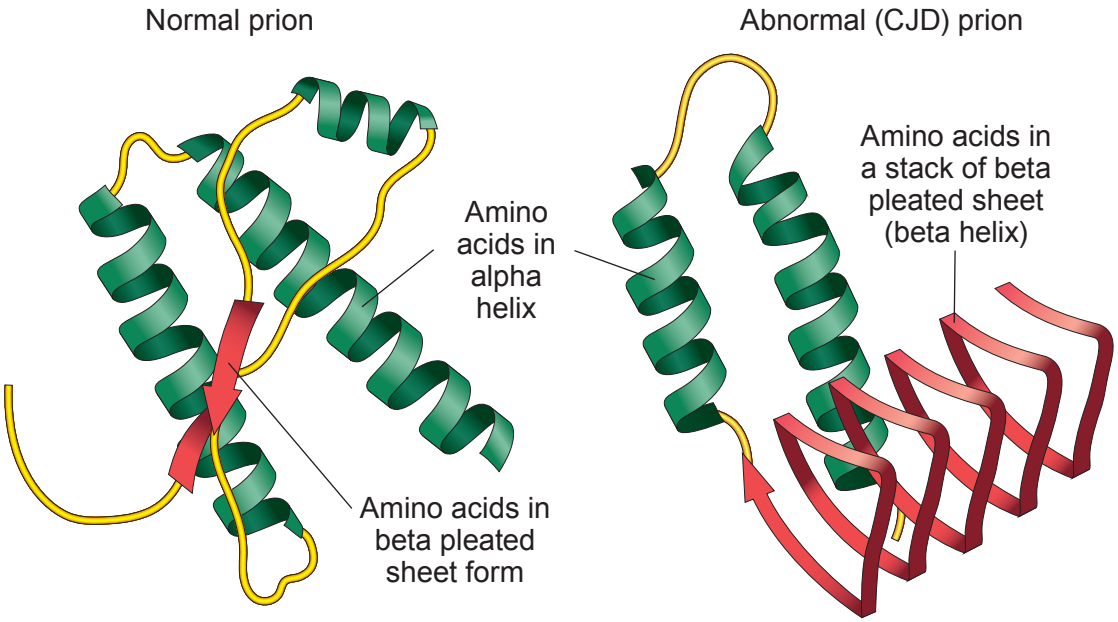


Figure 1: Structure of normal and abnormal (CJD) prion protein.

Types of CJD

There are four main types of CJD.

Sporadic CJD

This is the most common type of CJD. The cause of sporadic CJD is not fully understood but it has been suggested that a normal prion protein turns into an abnormal prion. Sporadic CJD usually occurs in adults between the ages of 45 and 74, with symptoms tending to develop between the ages of 60-65 years.

Even though it is the most common type of CJD, it is still very rare with only one or two people in every million being affected each year in the UK.

Variant CJD (vCJD)

This type of CJD is caused, most likely, by consuming meat from a cow that had bovine spongiform encephalopathy (BSE). BSE is a similar prion disease to CJD in humans.

In the mid-1990s the link between vCJD and BSE was discovered and since then controls have been in place to prevent infected meat entering the food chain.

The average time for symptoms of vCJD to occur after infection is unclear. The incubation period may be over 10 years, meaning people that were exposed to infected meat before the food controls were introduced could still develop vCJD.

The vCJD prion can also be transmitted via blood transfusion.

Inherited CJD

This type of CJD is a very rare genetic condition where the abnormal prion protein gene is inherited. A gene mutation results in abnormal prions forming in the brain during adulthood, and symptoms of CJD therefore develop.
In the UK, 1 in every 9 million people are affected by inherited CJD, with symptoms first developing when a person is in their early 50s.

Iatrogenic CJD

This type of CJD is where the infection is spread accidentally from someone with CJD through surgical or medical treatments.

In the past a common cause of iatrogenic CJD was growth hormone treatment. Human pituitary growth hormones were extracted from individuals that were deceased, some of these were infected with CJD. Since 1985, synthetic human growth hormones have been used so there is no longer a risk of infection.

During brain surgery, iatrogenic CJD can be spread if the instruments used on a person with CJD are not sterilised and cleaned properly between procedures.

Symptoms of CJD

Symptoms will depend on the type of CJD that a person is suffering from. The neurological and psychological systems are affected by CJD.

Most people with CJD die within 6-12 months of the initial symptoms.

Table 1: Possible neurological symptoms of CJD and to which type the symptoms are relevant.

Initial Symptoms Sporadic CJD	Advanced Symptoms All types of CJD	Final Stages All types of CJD
• difficulty walking, caused by balance and co-ordination problems • slurred speech • numbness in different parts of the body • dizziness • vision problems, such as double vision and hallucinations	• loss of physical co-ordination and ataxia • muscle twitches and spasms • loss of bladder and bowel control • blindness • dysphagia • loss of speech • loss of voluntary movement	• loss of mobility • lack of awareness of surroundings • loss of ability to speak • death often due to infection

Table 2: Possible psychological symptoms of CJD and to which type the symptoms are relevant.

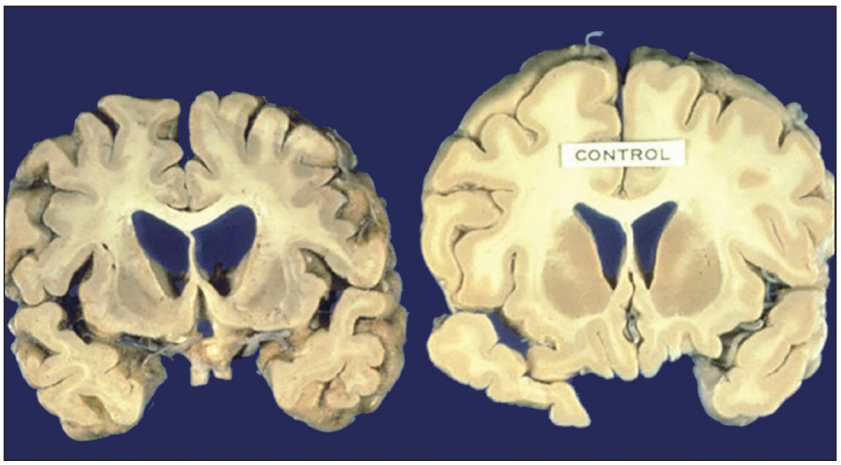
Initial Symptoms vCJD	Advanced Symptoms All types of CJD
• severe depression • intense feelings of despair • withdrawal from family and friends • anxiety • irritability • insomnia	• severe memory loss • confusion • feeling agitated • aggressive behaviour • loss of appetite • paranoia • unusual and inappropriate emotional responses

Diagnosing CJD

Diagnosis of CJD is often based on symptoms, a series of tests and medical history.

Neurologists will test patients to rule out other conditions that have similar symptoms such as Alzheimer's disease, Parkinson's disease or a brain tumor.

Brain tissue from CJD patient



Normal unaffected brain tissue

Figure 2: Brain tissue from a CJD sufferer compared to that of normal unaffected brain tissue.

Tests for CJD

Magnetic resonance imaging (MRI)

MRI uses strong magnetic fields and radio waves to produce a detailed image of the brain and can show up abnormalities that are particular to CJD.

Electroencephalogram (EEG)

An EEG records brain activity and may pick up abnormal electrical patterns seen in CJD.

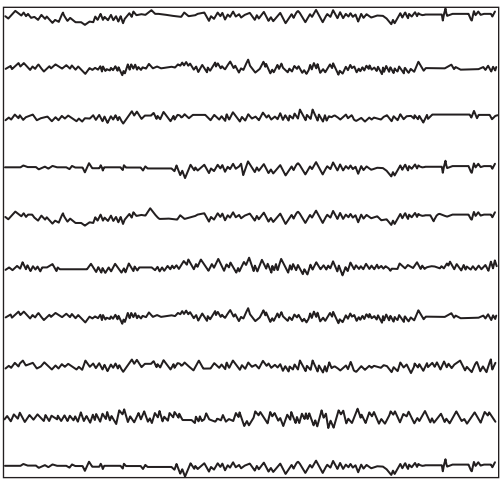


Figure 3: An EEG trace of a healthy individual

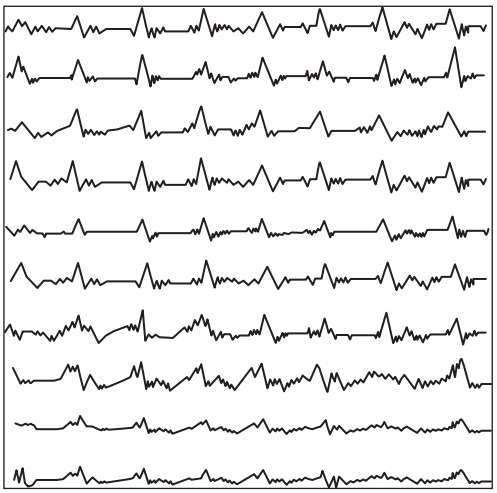


Figure 4: An EEG trace of a patient with CJD

Lumbar puncture

This is a procedure where a needle is inserted into the lower part of the spine to draw out a sample of the fluid which surrounds the brain and spinal cord (cerebrospinal fluid). The fluid can be tested for CJD prions.

Blood test

A prototype blood test was developed in 2016 to test for vCJD.

Tonsil biopsy

A small piece of tonsil tissue can be checked for abnormal prions found in vCJD. These prions are not found in other types of CJD.

Genetic tests

A blood test to find the presence of a prion gene mutation can be carried out. If there is a positive result then it can indicate inherited CJD.

Brain biopsy

A tiny hole is drilled into the skull and a small section of brain tissue is removed using a very thin needle. This is carried out under general anaesthetic so the patient is unconscious during the procedure.

The biopsy carries the risk of brain damage or seizures and is only performed in a few cases where there is concern that someone doesn't have CJD but some other treatable condition.

Treating CJD

Currently, there is no cure for CJD. The National Prion Clinic is investigating possible treatments and is carrying out clinical studies.

CJD sufferers are kept comfortable and symptoms are reduced through use of medication. Anxiety and depression are treated with sedatives and antidepressants. Muscle jerks and spasms are treated with clonazepam and sodium valproate. Pain is treated with opiate-based painkillers.

Advance directive for CJD sufferers.

This is where a person makes their treatment preferences known in advance in case they are unable to communicate their decisions later due to illness. People with CJD are referred to a specialist team that helps patients and their families with the advance directive.

The advance directive covers issues including:

- Treatment at home, in a hospice or in a hospital once they reach the final stages of the condition.
- The types of medication they would be willing to take in certain circumstances.
- Whether they would be willing to use a feeding tube if they can no longer swallow food and liquid.
- Whether they are willing to donate organs for research purposes after death.
- Whether they would be willing to be resuscitated if they have respiratory failure.

Preventing CJD

CJD is a rare condition which is difficult to prevent.

Surgical equipment guidelines

Guidelines on the reuse of surgical equipment means that cases of iatrogenic CJD spread through medical treatment are very rare.

Protecting food supplies

Strict controls on the sale of infected meat are now in place so the transmission of BSE to humans resulting in vCJD is limited. These controls include:

- A ban on feeding meat-and-bone mix to farm animals.
- The removal and destruction of all parts of an animal's carcass that could be infected with BSE.
- A ban on mechanically-recovered meat (meat residue left on the carcass that is pressure-blasted off the bones).
- Testing cattle more than 30 months old for BSE.

Blood supplies

There have been four known cases in the UK where vCJD has been transmitted by blood transfusion. These people received blood from a donor who later developed vCJD.

Three recipients went on to develop vCJD, while one died before developing vCJD but was found to be infected following a *post mortem* examination.

Steps have been taken to minimise the risk of the blood supply becoming contaminated, these include:

- Not allowing people potentially at risk from vCJD to donate blood, tissue or organs (including eggs and sperm for fertility treatments).
- Not accepting donations from people who've received a blood transfusion in the UK since 1980.
- Removing white blood cells, which may carry the greatest risk of transmitting vCJD, from all blood used for transfusions.

CJD Statistics

Graph 1: Number of probable vCJD deaths in selected countries, 1995-2011.

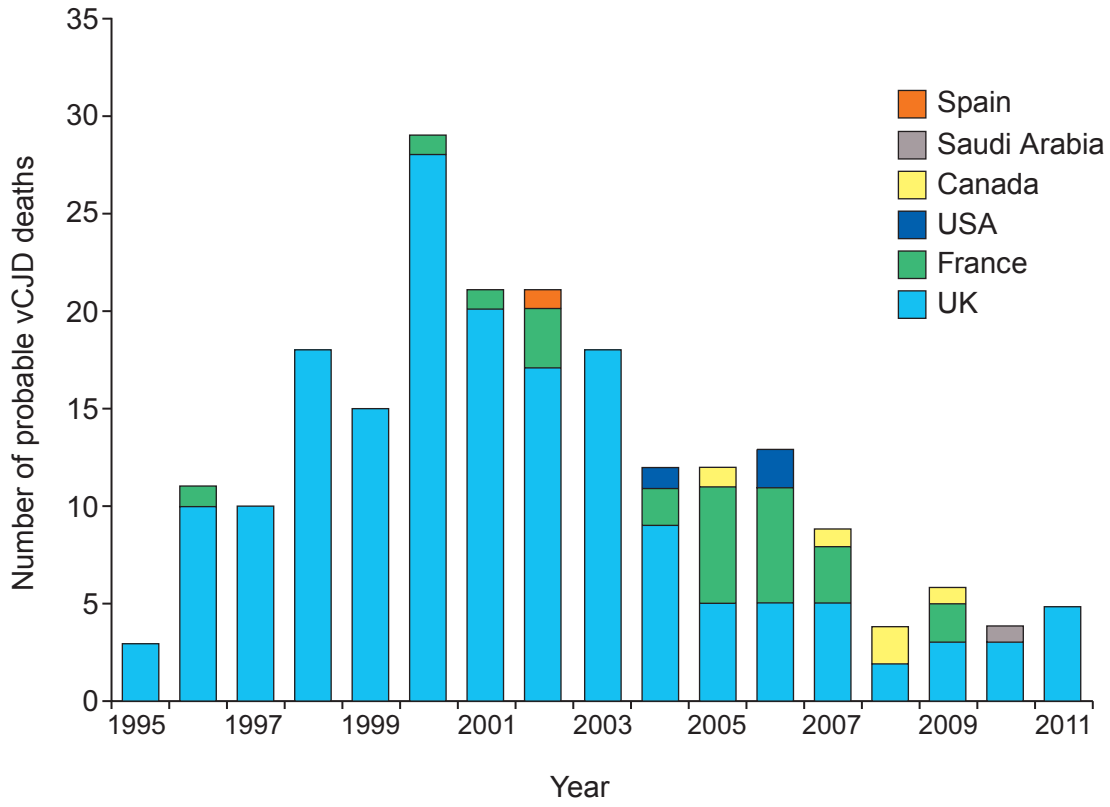


Table 3: The number of referrals and deaths from CJD in the UK between 1991-2014

		Deaths from CJD				
Year	Referrals of suspected CJD	Sporadic	Iatrogenic	Inherited	vCJD	Total deaths
1991	75	31	1	4	No data	36
1992	96	45	2	6		53
1993	79	36	4	7		47
1994	119	53	1	9		63
1995	87	35	4	5	3	47
1996	132	40	4	6	10	60
1997	163	59	6	6	10	81
1998	155	64	3	5	18	90
1999	170	62	6	2	15	85
2000	178	50	1	3	28	82
2001	179	58	4	6	20	88
2002	164	73	0	5	17	95
2003	162	79	5	6	18	108
2004	114	50	2	6	9	67
2005	124	67	4	13	5	89
2006	112	68	1	9	5	83
2007	119	64	2	10	5	81
2008	150	86	5	5	2	98
2009	153	80	2	8	3	93
2010	150	85	3	7	3	98
2011	158	91	4	14	5	114
2012	127	93	5	11	0	109
2013	151	107	2	8	1	118
2014	128	96	3	11	0	110
Total	**3 245**	**1 572**	**74**	**172**	**177**	**1 995**