Glossary of terms relevant to prion diseases

About the CJD Support Network

The CJD Support Network is the leading care and support charity for all forms of CJD. The CJD Support Network:

- Provides practical and emotional support to individuals, families and professionals concerned with all forms of CJD
- Provides emotional support to people who have been told that they are at a 'higher risk' of CJD through blood or surgical instruments
- Links families with similar experiences of all forms of CJD
- Offers financial support for families in need
- Provides accurate, unbiased and up-to-date information and advice about all forms of CJD
- Provides a national helpline on all forms of CJD
- Promotes research and the dissemination of research findings
- Promotes good quality care for people with all forms of CJD
- Encourages the development of a public policy response for all forms of CJD
- Provides support, education and training to professionals concerned with CJD

For more information about the activities of the CJD Support Network, contact:

Admin and general enquiries – admin@cjdsupport.co.uk or +44 (0)7494 211476
Support – support@cjdsupport.co.uk or 0800 774 7317
Website – www.cjdsupport.co.uk
Post - PO Box 3936, Chester, CH1 9NG

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14-3-3 A normal protein found in brain cells that is found in elevated levels in cerebrospinal fluid (CSF) in various brain diseases (including CJD) and brain trauma.

Akinetic Mutism A state of immobility and loss of speech that occurs in serious, widespread brain damage, such as occurs in the later stages of CJD.

Amino Acids Small molecules that link together to form proteins. There are many amino acids but only around 20 of them make up the proteins found in the human body. They are both named and given a single letter code. Three examples are: methionine with the letter code 'M', valine with letter code 'V', and lysine with letter code 'K'.

Amyloid A structure formed by aggregations of proteins with certain physical characteristics. Amyloid deposits may be seen in various diseases, including CJD.

Asymptomatic Infection An infection of an animal or human that is present in their body but which is not causing any symptoms; it is a 'clinically silent' infection. After any infection, there is always a period without symptoms, before significant disease develops and causes a clinically evident illness. With many infections, this period of asymptomatic infection is measured in hours or days, but it can be longer, and, in the case of prion diseases, it often extends into years. If the infected individual does become ill, this period of asymptomatic infection is termed the 'preclinical period' or the 'incubation period'. Some infections may remain permanently asymptomatic i.e. never cause disease in that individual and then the term 'asymptomatic infection' is the correct term.

Autopsy An examination of the body after death, usually undertaken to determine the cause of death. It may involve examination of all of the body or be limited to certain specific parts. In some neurological illnesses (such as CJD), it may be limited to examining the brain; this may involve looking at the whole brain or taking samples from parts of it.

Autosomal Dominance A specific pattern of genetic inheritance. Every person has two sets of genes: one from their father and one from their mother. In autosomal dominant genetic disease, if a person has one abnormal gene they are at risk of developing disease even though the other gene is normal. The result is that if one parent has one abnormal gene and one normal gene, while the other parent has two normal genes, each of their children has a 50:50 chance of inheriting an abnormal gene.

Biopsy Taking a sample of some body tissue in life, to look for a disease in that tissue. In neurology, a brain biopsy may be undertaken but this is done uncommonly, only in very specific situations.

BSE (Bovine Spongiform Encephalopathy)

A prion disease of cattle that was identified in the UK in the 1980s. It is one of a family of prion diseases affecting animals and humans. The origin of BSE is uncertain. There are now three recognised types of BSE: C,H,L. Variant CJD was related to the classical, C-type.

Cerebellar Ataxia

A set of symptoms and difficulties that result from disease of the cerebellum, a specific part of the brain that is mostly concerned with the coordination of movement. Symptoms include unsteadiness, falls, clumsiness, vertigo and slurred speech.

Chromosome

Each cell in the body contains a set of tiny structures called chromosomes (23 different chromosomes). The chromosomes contain genes which are strings of code that are instructions for making proteins. Two particular chromosomes (X and Y) are responsible for determining the sex of the individual. The gene for prion protein is on Chromosome 20.

CJD/Creutzfeldt-Jakob Disease

This is the commonest form of human prion disease. First described in the 1920s. Named after Dr A Jakob and Dr H Creutzfeldt. However, while Jakob certainly was the first to describe this disease, Creutzfeldt's name has been associated by historical accident.

Codon 129

A gene is a string of code units, with each unit being a code for one amino acid. With the string of code units laid out in a line, each code unit is a 'codon' and they are numbered from left to right. In PRNP (the prion protein gene), the 129th codon is of particular importance. In humans, there is a common variation in the code here, with Codon 129 being either the code for the amino acid methionine (M) or for valine (V). As humans have one set of genes from their father and one set from their mother, they have two sets of PRNP. If the codon 129 code is for methionine in both, they are 'Codon 129 MM', with the other possibilities being MV and VV. These variations at codon 129 do not have any direct disease consequences-they are all normal variations, but they can have effects on prion disease.

Cortical Blindness

A loss of vision caused by damage to the visual cortex of the brain. Other forms of blindness are due to problems with the eyes or optic nerves; in cortical blindness these structures are normal, but the part of the brain that creates the visual experience is damaged.

CSF (Cerebro-spinal fluid)

A fluid that surrounds the brain and spinal cord, filling the space between the brain and the skull and the space between the spinal cord and the bony spine.

CT (Computed Tomography)	A form of X-Ray imaging that allows much more detailed imaging than is possible with straightforward X-Ray.
CWD (Chronic Wasting Disease)	A prion disease of Cervids (for example, mule deer, white-tailed deer, elk, moose), first identified in USA but identified now in USA, Canada & Norway, with single cases having been identified in Finland & Sweden. Not yet identified in any UK deer species. It spreads relatively easily within deer populations. It is not yet proven to be a risk to human health.
Diagnostic Criteria	A set of formal criteria that need to be fulfilled for a specific diagnosis. They may be used in routine clinical practice but are mostly designed in relation to consistency in disease surveillance and research.
EEG (electroencephalogram)	A means of recording the electrical activity of the brain via small electrodes placed on the scalp.
Encephalopathy	A disease of the brain. It may be due to a direct disease process in the brain tissue or due to brain dysfunction because of disease elsewhere in the body.
FFI (Fatal Familial Insomnia	A form of human genetic prion disease that is so named because sleep disturbance is a prominent feature and, being genetic, runs in families. It is caused by a particular gene mutation D178N: at codon 178 of PRNP, the code for the amino acid asparagine (N) is present rather than the code for aspartic acid (D). Some authorities feel that genetic prion disease is best referred to as simply genetic with the responsible mutation then specified (for example: genetic prion disease; D178N), rather than using historical terms such as 'FFI'.
Florid Plaque	A pathological feature seen in the brain: a form of prion protein deposition with surrounding spongiform change. Most typically seen in variant CJD.
GSS (Gerstmann Sträussler Sheinker) disease	A form of human genetic prion disease that is named after the original describers. The original description was of an illness presenting with cerebellar ataxia and the main underlying PRNP mutation is P102L: at codon 102, the code for amino acid proline (P) being replaced by the code for leucine (L). However, the term GSS has been applied to prion disease resulting from other mutations and with a somewhat variable clinical picture, leading to a slightly confusing situation. Some authorities feel that genetic prion disease is best referred to as simply genetic with the responsible mutation then specified (for example: genetic prion disease; P102L), rather than using historical terms such as 'GSS'.
Glia	The brain contains various types of cells. Glial cells are one type.

Iatrogenic Literally, 'caused by doctors'. An iatrogenic disease is one contracted via medical or surgical procedures.

Immunochemistry A specific method of staining proteins in tissues. Immunochemistry can determine that a particular protein is present in a tissue and show how it is distributed. In prion disease, it can show the presence of prion protein and show the presence of plaques and other patterns of distribution.

Incubation Period In infections, the time between being infected and actually developing symptoms of the resulting infectious disease.

Kuru A form of human prion disease that affected certain populations in the Eastern Highlands of Papua New Guinea. Transmitted from person to person via consumption of human tissue during traditional mourning rituals.

LP (Lumbar Puncture) A procedure for obtaining a sample of CSF. Local anaesthetic is used to allow the passing of a fine needle into the lower back in order to obtain CSF from the bottom part of the spinal canal.

Lymphoid Tissue Tissue that is part of the immune system including: lymph nodes, tonsils, the appendix, spleen and Peyer's patches in the intestines.

Misfolding Proteins (see below) begin life as long molecules consisting of a string of basic chemical units (called amino acids). However, this is the basic ('primary') structure. After the amino acid chain is formed, it undergoes various modifications. One important modification is the folding of this klong chain into complex 3-dimensional shapes. The final structure of the protein is important for its functions. However, the protein can 'mis-fold' into a different shape and this is important in certain diseases, such as prion disease.

MRI MRI (Magnetic Resonance Imaging) is a form of imaging that involves magnetic fields rather than X-Rays. It gives much better images of the brain and spinal cord than X-Ray based imaging.

Mutation (genetic) An abnormality in a gene (part of the code is different from normal). A mistake in the gene code will lead to a change in the relevant protein. If this change is significant, it may affect the protein's function and cause disease. Strictly speaking, a 'mutation' is simply a change in the code and is not necessarily linked to disease (mutations are the driver of evolution) and the more specific term 'pathogenic mutation' (disease-causing mutation) is more accurate. However, in general discussion of genetic disease, the simple term 'mutation' is often used. Mutations in the prion protein gene are the cause of genetic prion disease.

Myoclonus

Brief, jerking movements that may affect parts of the body or the whole body. Myoclonic jerks are seen in normal situations, such as sometimes when falling asleep. However, they may occur in some diseases and are a particular characteristic of many prion diseases, especially in the later stages.

Neurodegenerative disease

A term that is used to describe certain neurological diseases that have the following characteristics:

1. They are age-related; mostly affecting the middle-aged and elderly.
2. They are due to neurons (nerve-cells) malfunctioning and dying
3. They are associated with the deposition of abnormal forms of normal proteins in brain tissue.
4. They are mostly of unknown cause, occurring sporadically in the population, but a minority of cases are genetic.

They include Alzheimer's disease, Parkinson's disease, Motor Neuron disease and sporadic CJD. Each disease is associated with specific proteins (for example, Parkinson's with alpha-synuclein; CJD with prion protein).

Neuron

A form of cell that is the basis of processing and communication within the nervous system. It is electrical in nature, able to transmit electrical impulses along its structure. Neurons control movement, allow sensation, interpret sound and light (hearing and vision), and are responsible for all of our mental functions.

Peyer's Patches

Small patches of lymphoid tissue in the wall of the small intestines. Part of the body's immune system. Thought to be important in the initial stages of prion infection via dietary BSE contamination.

Plaque

Plaques, in this context, are small areas of aggregated abnormal protein seen in the brain in certain diseases. Plaques consist of aggregated abnormal prion protein in prion diseases.

PMCA

Protein Misfolding Cyclic Amplification is a laboratory technique used to amplify the amount of an abnormal protein that may be present in a body fluid or tissue so that it becomes detectable by the usual detection techniques. These detection techniques work only if there is a sufficient amount of the abnormal protein present; very small amounts may be undetectable. It was developed as a means of amplifying the amount of abnormal prion protein present in tissues in prion disease. Its method is to add normal prion protein to a sample and then to encourage the process whereby any abnormal prion protein present converts the normal protein into abnormal protein. It is done in cycles to progressively increase the amount of abnormal prion protein. Another amplification method is RT-QuIC, but these two methods are different techniques and they behave differently in different prion diseases.

Preclinical Infection See 'Incubation Period' and 'Asymptomatic Infection' above.

Prion Strictly speaking, the 'prion' is the infectious agent or particle responsible for transmitting prion diseases when they occur as infections. The precise structure of the prion is not yet determined but it is thought to consist, mostly or entirely, of abnormally folded prion protein. In contrast to other infectious agents, it does not contain DNA or RNA and is considered to be a 'protein-only' agent.

Prion Disease Diseases of animals and humans that are associated with abnormal folding of prion protein, its deposition in tissues and resulting neuronal death. These are progressive brain diseases.

PRNP The gene on Chromosome 20 that is responsible for prion protein. Human genes are usually denoted by capital letters in italic script, as in *PRNP*.

Protein A class of molecules made up of chains of amino acids that have important roles in the structures and functions of the body.

Polymorphism A variation in genetic code that is not directly disease causing. For example, there is the common variation in code at codon 129 of the prion protein gene, *PRNP*.

Prion Protein One of the normal proteins of the body which is found in various tissues, but particularly in the brain.

Pulvinar Sign A feature of the brain MRI typically seen in variant CJD. The pulvinar is a part of the thalamus, which is a important group of neurons in the central part of the brain. In vCJD, it shows up as a brighter than normal area on the scan.

RT-QuIC Real Time-Quaking Induced Conversion is a laboratory technique used to amplify the amount of an abnormal protein that may be present in a body fluid or tissue so that it becomes detectable by the usual detection techniques. These detection techniques work only if there is a sufficient amount of the abnormal protein present; very small amounts may be undetectable. It was developed as a means of amplifying the amount of abnormal prion protein present in tissues in prion disease. Its method is to add normal prion protein to a sample and then to encourage the process whereby any abnormal prion protein present converts the normal protein into abnormal protein. Another amplification method is RT-QuIC, but these two methods are different techniques and they behave differently in different prion diseases. The RT-QuIC CSF test is very helpful in the diagnosis of sCJD.

Scrapie — A prion disease of sheep and goats.

Spongiform Change — A spongy appearance of the brain that is seen in prion diseases, related to the loss of neurons that occurs in the disease.

Sporadic CJD — The commonest form of human prion disease. It is of unknown cause and appears in all countries at the same sort of frequency. Since it occurs more or less randomly in the population, it occurs sporadically, hence its name.

SFI (Sporadic Fatal Insomnia) — This is a term that some authorities favour and some do not. It refers to a form of sporadic CJD that has clinical features similar to those of FFI but occurs sporadically and is not due to an underlying, inherited, mutation.

Synapses — Neurons communicate with each other. The communication junctions between neurons are called 'synapses'. Although information is conveyed electrically within neurons, the transmission between neurons is via chemicals ('chemical transmitters'). The electrical impulse in the neuron arrives at the synapse and causes a chemical to be released which travels to the next neuron and, there, triggers an electrical impulse in the receiving neuron. These connections are of prime importance to the functioning of the neuronal networks that form the brain. Because the transmission is chemical, it means that neuronal communication can be altered by drugs. Synapses are often important starting points for neurological disease.

Tau — A normal body protein with important functions in the brain. It may be found at elevated levels in CSF in some neurological diseases.

(TSE) Transmissible Spongiform Encephalopathy — Another name for prion diseases, coined before the prion protein nature of these diseases was understood. 'Encephalopathy": brain disease. 'Spongiform': the characteristic spongy brain change seen in prion diseases. 'Transmissible': referring to the fact that prion diseases can be transmitted in certain circumstances.

VPSPr (Variably Protease Sensitive Prionopathy) — Essentially a form of sporadic CJD, in that it is a sporadic human prion disease. It has some different prion protein characteristics: in typical sCJD, the abnormal prion protein is relatively 'protease resistant', whereas in VPSP, the abnormal prion protein is variably protease sensitive. Proteases are chemicals that break down proteins. The clinical features of VPSPr are varied but essentially present as progressive brain diseases.

Further information and contacts

Further information about CJD may be found on the CJD Support Network website at www.cjdsupport.co.uk, our fact sheets are also available by post on request to the Network.

Support and information may be obtained from the organisations below:

CJD Support Network

Address – PO Box 3936, Chester, CH1 9NG
Website – www.cjdsupport.co.uk
Phone – 0800 774 7317
Email – admin@cjdsupport.co.uk or support@cjdsupport.co.uk

National CJD Diagnostic Advisory Service

Based at the Royal Infirmary of Edinburgh
Website page with contact information - www.cjd.ed.ac.uk
Email - loth.securecjd@nhs.scot

UK National CJD Nursing Service/National Care Fund

Address - Department of Clinical Neurosciences, Clinical Offices, 2nd Floor
50 Little France Crescent, Edinburgh Bio-Quarter, Edinburgh, EH16 4TJ
Website – www.cjd.ed.ac.uk
Phone - 0131 312 0193 / 0131 312 0192
Email - Terri Awe (primary contact) – terri.awe@nhs.scot, Juli Jose (additional contact) juli.jose@nhs.scot

National Prion Clinic

Address - National Prion Clinic, Institute of Prion Diseases, Courtauld Building, 33 Cleveland Street, London, W1W 7FF
Website - www.ucl.ac.uk/national-prion-clinic
Phone - 020 7679 5142 / 020 7679 5036
Email - uclh.prion.help@nhs.net