Name of disorder: Creutzfeldt-Jakob disease
Essay title: Creutzfeldt-Jakob disease: When a good protein turns bad
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Creutzfeldt-Jakob disease (CJD) is a rapidly progressive neurological disease and is part of a group of rare diseases known as transmissible spongiform encephalopathies (TSEs) or prion diseases. Prion diseases affect both humans and animals and includes the infamous bovine spongiform encephalopathy (BSE), more commonly known as 'mad-cow disease' and the human form of the disease, variant CJD (vCJD). CJD was first identified in humans in the 1920's. It wasn't until the 1980's, however, that the causative agent, the prion protein was identified. Under disease free conditions the prion protein is a normal functioning protein found in the body's cells, however, in prion diseases this protein adopts an abnormal conformation and aggregates causing neuronal cell death. The misfolded prion protein is unique as it is highly resistant to treatments that usually destroy viruses and bacteria. How or why the prion protein undergoes conversion to its disease-associated form still remains elusive and is currently a major research focus.

There are three major etiologies of the disease: sporadic CJD, genetic CJD and acquired CJD. Sporadic CJD accounts for about 90% of cases with an annual global incidence of 1-2 cases per million per year and appears even though the person has no known risk factors for the disease. Sporadic CJD most often affects people between the ages of 50 to 70 years of age and the median survival is only around 4 months. Genetic CJD on the other hand occurs in about 5-10% of cases and is caused by a genetic mutation in the prion protein gene, *PRNP*. The mean age at onset is slightly younger and illness duration is longer than sporadic CJD. Acquired CJD results from contraction of the disease through medical procedures such as hormone or graft treatments, neurosurgery and blood transfusions, or in the case of vCJD, through ingestion of meat products contaminated with BSE. In contrast to sporadic CJD, vCJD affects significantly younger age group and progresses more slowly. Symptoms of CJD are varied but can include confusion or disorientation, cognitive impairment, mild psychiatric symptoms including mood changes, anxiety, malaise and diminished ability to concentrate, loss of balance and muscle control causing difficultly walking, muscle spasms and visual impairment including double vision or blindness. In vCJD, there is usually a predominance of psychiatric and behavioral symptoms rather than a progressive dementia. From the onset of symptoms the disease can progress very quickly and ultimately leads to a vegetative state followed inevitably by death.

Diagnosis of CJD is highly complex and is a combination of clinical history, neurologic examination and clinical testing. Four clinical tests are widely used for the diagnosis of CJD: electroencephalographs (EEG) recording, CSF analysis of the 14-3-3 markers, tau and the prion protein, brain biopsy and brain MRI. Sequencing of the *PRNP* gene is done to search for a mutation when the inherited form is suspected. Although examination of brain tissue obtained by biopsy remains the only way to confirm the diagnosis of sporadic CJD in living patients, this highly invasive test can often be avoided as careful neurologic examination and interpretation of the other diagnostic tests can result in an accurate and timely diagnosis. Because there is no treatment or cure for CJD, current treatment is aimed at alleviating symptoms and making the patient as comfortable as possible. Opiate drugs can help relieve the pain and the drugs clonazepam and sodium valproate may help relieve involuntary muscle jerks.

More reliable diagnostic approaches for CJD are currently being developed and clinical trials of anti-prion antibodies for immunotherapeutic treatment of the disease will begin soon in the UK.