REVIEW OF ACTION TAKEN TO PREVENT THE THEORETICAL RISK OF PERSON-TO-PERSON TRANSMISSION OF NEW VARIANT CREUTZFELDT-JAKOB DISEASE: ADVICE TO HEALTH MINISTERS

PURPOSE

The purpose of this memorandum is to take stock of the action already taken on a precautionary basis to prevent the theoretical risk of transmission of new variant Creutzfeldt-Jakob Disease (nvCJD) from person-to-person. Areas where the need for further action is being considered are also identified.

THE DISEASE

New variant Creutzfeldt-Jakob Disease (nvCJD) was first recognised in 1995 when the National CJD Surveillance Unit in Edinburgh identified a previously unrecognised form of CJD – generally a younger age at onset, different symptoms at presentation, and a distinctive appearance of brain tissue on pathological examination. Many scientists, as well as the Spongiform Encephalopathy Advisory Committee (SEAC), believe that the most likely explanation for this disease is that it has been caused by eating parts of cattle infected with Bovine Spongiform Encephalopathy (BSE). To date there have been 35 definite and probable cases of the disease. It is impossible to predict the number of cases which will eventually occur. At this time, the estimates, compatible with the present number of confirmed cases, range from under a hundred to several million.

Classical CJD has been recognised for around 80 years and has so far been rare, occurring during the last few years at an annual average of 32 in Great Britain. Its causation is unknown.

Both nvCJD and Classical CJD are human forms of a group of diseases called transmissible

spongiform encephalopathies, which affect animals and people. The diseases include BSE in cattle and scrapie in sheep. The leading theory as to the agent responsible for causing them is the 'prion protein theory'. This theory holds that abnormal prion protein causes the normal prion protein which is found in the tissues of healthy people and animals to change its shape and leads to the destruction of nervous tissue in the brain, giving it a spongy appearance under the microscope.

[DN: Commentary on the likely size of the epidemic drawn from respected research papers].

BASIS OF THE CONCERN

The concern that there may be human-to-human transmission of nvCJD through medical care has arisen because of a number of observations:

- Rarely, in the past, classical CJD has been spread from person-to-person following medical treatment involving the brain or central nervous system (CNS).

- Under experimental conditions some peripheral (i.e. non-nervous) tissue taken from people with classical CJD has been shown to be capable of infecting animals.

- Human Growth Hormone has transmitted classical CJD on 100 occasions worldwide.

- Abnormal prion protein has been found in the appendix of a patient who later developed nvCJD.

- Abnormal prion protein has been found in the tonsils of a group of patients alive with clinical signs of nvCJD and in the lymphoreticular tissue of those who had died from the disease.

- It is not known how nvCJD migrates within the body of an infected person but it may be via white blood cells. **[DN: reword].**

- There is no species barrier. **[DN: reword]**

  [DN: Any other bullet points]

Thus, the basis of the concern that nvCJD might be transmitted from person-to-person via medical procedures has two main elements. Firstly, that it has been demonstrated that classical CJD can be transmitted via surgical instruments even after they have had multiple sterilisations. Secondly, that nvCJD has a different distribution in human tissues than classical CJD and appears to be present in lymphatic tissue before it invades the nervous system. The risk remains theoretical because transmission of nvCJD has not yet been demonstrated from patient-to-patient after treatment, nor experimentally.

- **RELEVANT RESEARCH AND CLINICAL EVIDENCE**

Considering these concerns, the relevant research data and clinical reports providing evidence for transmission of TSEs is as follows:

a. **Transmission of Classical CJD by medical means**

Transmission of classical CJD from an infected patient to subsequent patients by surgical procedures has been reported over many years: three cases transmitted by contaminated neurosurgical instruments in Britain in 1955; two cases transmitted by contaminated brain electrodes in Switzerland in 1977; three cases transmitted by grafts of the cornea since 1974 worldwide. There have been 69 cases associated with dura mater grafts (mostly in Japan), of which six have been in the United Kingdom. In addition over 100 cases of classical CJD associated with human growth hormone (HgH) treatments have been reported worldwide; and 28 people have died in the United Kingdom alone from HgH-related CJD.

a. **Transmission of nvCJD by medical means**

There have been no cases reported as yet in the world's literature of transmission of nvCJD by medical procedures or from person to person by other means.

a. Transmission of TSEs within animal species

TSEs have been reported to occur naturally in sheep and goats (scrapie) and deer (chronic wasting disease (CWD)). TSEs associated with feed have been reported in cattle (BSE), domestic cats, captive wild cats, captive exotic ruminants, farmed mink (Transmissible Mink Encephalopathy (TME)). Brain tissue from cases of TSE disease has been shown to transmit infection by intracerebral inoculation into a number of animal species including primates. **[DN: Intraperitoneal?]** Oral transmission of BSE has been demonstrated in mice, sheep, goats, mink and cattle.

PRECAUTIONARY CONTROL MEASURES ALREADY IN PLACE OR BEING IMPLEMENTED

The following control measures to prevent the risk of person-to-person spread of Classical CJD and to prevent the theoretical risk of transmission of nvCJD are in place or are being implemented.

c. Reduction of risk of transmission via surgical instruments

[DN: rework to show chronology of control measures which have been put in place].

There are two categories of surgical instrument, single use and reusable. Advice is that single use devices should be discarded after an episode of use. For re-usable instruments, the Department has published best practice guidance for decontamination. This is in the form of Health Technical Memoranda (HTMs) for sterilisation and washer-disinfectors (NHS Estates). Generic guidance on decontamination is available from the Medical Devices Agency.

The best practice guidance ("Sterilization, Disinfection and Cleaning of Medical Equipment: Guidance on Decontamination", from the Microbiology Advisory Committee to DH and MDA) recommends that surgical instruments are thoroughly cleaned by a process of demonstrated effectiveness and then subjected to a conventional sterilization process. This provides assurance of inactivation of conventional micro-organisms and

reduces the risk of transmission of CJD.

Since 1981, instruments once used on a CJD patient for procedures involving the brain, spinal cord or eye cannot be used on subsequent patients (guidance issued by the Department of Health and Social Security, DA (81)22). In 1992, this advice was extended, by PL(92) CO/4, to patients categorised as being at risk of developing CJD (recipients of human pituitary derived hormones, recipients of dura-mater grafts and people with a family history of familial CJD).

Reduction of risk of transmission via blood

[DN: Describe more fully with source of advice, dates, Ministerial announcements].

- Potential donors with risk factors for iatrogenic and classic CJD are excluded from giving blood. Various exclusions have been introduced over the past 10 years (eg people who received human growth hormone (1989); people with a family history of CJD (1996); people who have had cornea transplants (1997); people who had brain surgery or an operation for a tumour or cyst on the spine before August 1992 (April 1998).

- The National Blood Authority were instructed to lecuodeplete the blood supply in July 1998 following advice from SEAC. Leucopdepletion - the removal of white cells from blood and blood components - should reduce the risk of nvCJD infection through blood transfusion. All platelets and around 10% of red cells are now leucodepleted. Universal leucodepletion of blood for transfusion will be in place by October, 1999;

- Following advice from the Committee on Safety of Medicines in February 1998 (confirmed in May 1998), the Bio-Products Laboratory began importing plasma for the manufacture of plasma-derived blood products, eg Factor 8 and 9, albumin. immunoglobulin. This should eliminate any risk there may have been from infectivity in these products. All mainstream blood products from the Bio-Products Laboratory (BPL) are now manufactured using non-UK plasma. Hyperimmune products (including Anti-D) will follow in April 1999. A commercially produced

Anti-D product, using non-UK plasma has been available in the UK for some time but in short supply. The Committee on Safety of Medicine has recently (February 1999) licenced a second Anti-D product manufactured outside the UK, which should improve the supply.

- **Medicines**

DN – statement on use of human derived material in medicines

Medical Devices

DN – statement on use of human derived material in medical devices

Tissues for transplantation

DN – anything to say

FURTHER MEASURES UNDER CONSIDERATION

a. **Extension of control measures on surgical instruments**

Given the theoretical risk of transmission of nvCJD via surgical instruments which have been in contact with lymphoreticular tissue, the Spongiform Encephalopathy Advisory Committee (SEAC) has been asked to review its advice at its next meeting. In preparation for this meeting, Department of Health officials have: commissioned work on a risk assessment; had discussions with a panel of surgeons about the practicalities for some surgical practice of using more disposable instruments; sought advice from the Medical Devices Agency about the scope for substitution of re-usable instruments with disposable instruments; initiated discussions with the manufacturers of surgical instruments to explore the feasibility of unique labelling of instruments so that tracing will be easier in the future.

a. **Strengthening sterilisation and decontamination methods**

Insert details

a. Establishing the prevalence of abnormal prion protein in the population

Insert details

a. Research to identify a presumptive diagnostic test and a treatment for nvCJD

Insert details

a. Other measures

Insert details

CONCLUSIONS

1. Classical CJD has been shown on many occasions worldwide to have been transmitted from person-to-person via medical procedures such as neurosurgery (via surgical instruments or brain electrodes), by injection of human growth hormone, and via grafts of nervous tissue (taken from one patient and used to treat another).

1. Such transmission is rare but Classical CJD is a rare disease. The risks are likely to be higher with a form of CJD which is commoner. It is too early to say whether nvCJD will result in a large number of cases but it may.

1. The agent which is believed to cause nvCJD, seems to be more widely distributed in the tissues of people with the disease. It affects the lymphatic tissues, and possibly does so before the disease invades the brain. This is a different pattern of infection to Classical CJD which does not appear to affect peripheral (i.e. non-nervous) tissue in this way. White blood cells may also be implicated in the spread of infectivity within the body.

1. Risk reduction measures have been taken against the theoretical possibility that

nvCJD could be transmitted by blood transfusion or blood products. Action to remove white cells (leucodepletion) from blood for transfusion will be fully implemented by October 1999. Blood products – including anti-D - from non-UK plasma will be in place by April/May 1999. A procedure was established in 1997 via the CJD Surveillance Unit in Edinburgh to notify the National Blood Authority of any CJD patient who had been a blood donor so that if possible their blood can be removed from the blood supply chain.

[DN: insert further conclusions in a similar vein]