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Dear Colleague

An integrated approach to human transmissible spongiform encephalopathies (prion diseases): surveillance, health care, public health controls, clinical trials and other clinical research.

The first UK clinical trial of potential therapy for Creutzfeldt-Jakob Disease (CJD) is expected to begin shortly. We need to ensure a high level of patient referral to the trial whilst maintaining the public health surveillance function, and delivery of the care package for patients with this disease.

The responsibility for care and investigation of individual patients remains with the consultant responsible for that patient in consultation with the general practitioner. Nevertheless, the Department of Health is asking the local consultant neurologist, or consultant in other speciality with responsibility for the patient's care, to report to both the National CJD Surveillance Unit and the National Prion Clinic all suspect cases of CJD and other prion diseases. Both the National CJD Surveillance Unit and the National Prion Clinic are able to provide clinical advice about individual patients.

It is essential that local consultants continue to report patient details, with consent, to the National CJD Surveillance Unit for public health and surveillance purposes. In addition, consultants will also wish to ensure that the patient and his or her family, carer or independent representative are put in touch with the national care package co-ordinator, based at the National CJD Surveillance Unit, who can facilitate access to local support services.

Simultaneously, local consultants are asked to report patient details, with consent, to the National Prion Clinic, so that patients can be offered the chance to participate in the PRION 1 trial, should the diagnosis be confirmed as probable or definite CJD or another prion disease, and also to participate in related research programmes. Completed forms should be faxed to the units, contact details are provided in Annex D. Referring

consultants may also wish to utilise the specialist clinical and diagnostic expertise at the National Prion Clinic.

The report to the National CJD Surveillance Unit and the National Prion Clinic should take place on a single form (attached at Annex A) and must be authorised by the patient or their representative. Patients/families should be provided with a single information leaflet explaining the work of both the National CJD Surveillance Unit and the National Prion Clinic. A copy, produced jointly by the two units, is at Annex B.

Annex C aims to clarify roles and responsibilities for the reporting, surveillance, diagnosis and care of patients with CJD and other transmissible spongiform encephalopathies, as well as arrangements for public health control measures and research. Contact details are at Annex D.

Actions requested of local clinicians

On encountering patients whom they suspect to be suffering from CJD, or a related prion disease, consultant neurologists (or other clinicians) will:

- complete the national reporting form and obtain consent from the patient, lead relative or carer/patient representatives;
- fax or post the completed form, with consent, to the National CJD Surveillance Unit and the National Prion Clinic;
- advise the patient, carer, or independent representative that staff from the National CJD Surveillance Unit will visit the patient for national surveillance purposes (with their consent). They will also be given the opportunity to participate in research programmes operated by the Unit should they so wish;
- consider utilising the expertise in diagnosis and management of patients offered by staff at the National Prion Clinic;
- advise the patient, carer or independent representative that staff from the National Prion Clinic will visit and offer the opportunity to participate in therapeutic trials and/or other clinical research programmes, should they so wish.
- make available samples of blood and Cerebrospinal Fluid (CSF), and the results of Magnetic Resonance Imaging (MRI) scans to the two units.

Conclusion

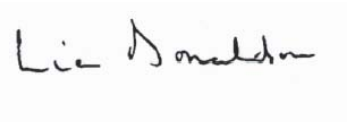
Maintaining high levels of public health protection from the risks of vCJD and other prion

diseases, ensuring high quality care for p atients with the disease, their families and carers, as well as furthering understanding of prion disease

and pursuing the goal of effective treatments for these fatal diseases depend on all individuals and organisations working well together.

This letter and its annexes are intended to clarify and strengthen arrangements to make sure that this happens.

Yours sincerely



SIR LIAM DONALDSON
CHIEF MEDICAL OFFICER

ANNEX A: National CJD Reporting Form

Fax to:

Family, carer or independent representative details (if appropriate*)

***** This may be appropriate if the approach is made via a lead family member, carer or independent representative (i.e. when a patient is too ill to be approached directly or has a preference for this route).

Surname:…… Forename(s):……

Postal Address:……
……
……
Postcode:……

Telephone number:……

Fax Number:……

Email Address:……

Patient details

Surname:…… Forename(s):……

Postal Address:……
……
……
Postcode:……

Telephone number:……

Fax Number:……

Email Address:……

NHS Number, if known:……

Brief clinical details: (please attach recent letter or discharge summary)

……
…… **Neurologist**

details (or other hospital clinician)

Surname:…… Forename(s):……

Hospital Postal Address:……
……
……
Postcode:……

Telephone number:……
Fax Number:……

GP Details

Surname:…… Forename(s):……

GP Practice Postal Address:……
……
……
Postcode:……

Telephone number:……
Fax Number:……

CCDC details

Surname:…… Forename(s):……

Postal Address:……
……
Postcode:……

Telephone number:……

Consent:

*please delete as appropriate

I have been provided with the patient information leaflet which explains the roles of the National CJD Surveillance Unit and the National Prion Clinic.

I agree to my/the patient's* details being forwarded to the National CJD Surveillance Unit and the National Prion Clinic.

I agree that staff from the National CJD Surveillance Unit in Edinburgh and the National Prion Clinic in London can visit myself/the patient* and my/their* relatives at a mutually convenient time for clinical assessment and surveillance purposes and to provide the opportunity, should we wish, to discuss ongoing research, including clinical trials of potential treatments.

I understand that this may mean providing further information to help in the organisation of my/the patient's* care, and to contribute to a better understanding of the illness.

Signed:……

Print:……

Date:……

On completion, please fax to NPC, 0207 3448 4046 NCJDSU 0131 343 1404, and also to your local CCDC.

Annex B: Patient information leaflet

PATIENT/CARER INFORMATION SHEET

WHY HAVE I RECEIVED THIS INFORMATION?

You are being given this information because the possibility of CJD or another form of prion disease is being considered. Two major, publicly funded, specialist teams work in the UK on these diseases. With your consent, someone from each team would like to visit you/the patient and discuss how they can help and also to discuss important research they are doing into the causes of, and treatments for, prion diseases.

Some people referred to these teams will turn out not to have prion disease. Whatever diagnosis is confirmed, your/the patients' care will be lead by your local clinical service. Involvement in any research is entirely voluntary and refusal to participate will not affect your care in any way.

WHO WILL BE APPROACHING ME?

1) The National CJD Surveillance Unit team

Western General Hospital, Edinburgh
Tel: 0131 537 2128
http://www.cjd.ed.ac.uk/

The National CJD Surveillance Unit (NCJDSU) is funded by the Department of Health to identify, classify and investigate prion diseases in the United Kingdom. The NCJDSU team will want to visit to make sure that it is a prion disease and also to identify what type of prion disease may be affecting you/the patient. They will also wish to discuss other research projects. The team consists of a doctor and a nurse who will travel to see you/the patient and to discuss things with the local clinicians. They can provide advice, guidance and diagnostic tests to help the doctor looking after you/the patient both in making the diagnosis and in giving care. A National Care Team is based at the NCJDSU. If you and the local clinicians wish, a care co-ordinator from the National Care Team will visit later to assess your/the patient's care needs and to help you and the local doctors to identify ways to meet these needs if they are not already met.

2) The National Prion Clinic and MRC Prion Unit treatment (clinical trial) team

National Hospital for Neurology and Neurosurgery, London
Tel: 020 3448 4037
http://www.uclh.nhs.uk/prion

The National Prion Clinic offers specialist in- and out-patient services including diagnostic facilities which are available to help support your doctors, if they wish, in choosing the best type of care for you as well as providing specialised advice and counselling.

A major, long-term, research effort is underway at the MRC Prion Unit in London to find new treatments for prion disease and to study if these treatments benefit patients (the MRC Prion-1 trial). We need to understand better how these rare diseases progress in everyone, not just those taking a new drug(s), in order to make real progress towards an effective treatment. Therefore, the Prion-1 trial has been designed to allow all patients that want to participate to do so, irrespective of whether or not they want to try the drug being tested at that time, or what form of prion disease they might have. The Department of Health has made a major financial investment in the trial and asked the Medical Research Council, which has over 50 years experience running trials, to find the best treatments for these diseases. The team would like to visit you to discuss the treatment trial and other research projects aimed at tackling these diseases.

IS THERE ANYONE ELSE I CAN TALK TO?

Many patients and carers find it helpful to talk to others with experience of the same diseases. There are two UK support groups for patients with prion disease and their families and carers. Both have confidential helplines, offering support and practical information. They each have a website, and regular newsletters, with lots of useful information.

Because these diseases are very rare, many local medical and care services have no experience of them. But you are not alone. The support groups, together with the specialist centres, are committed to making sure you don't miss out on whatever help is available. You don't have to wait until you have a firm diagnosis - support is there, if you want it, from the moment you have to consider the possibility of prion disease.

The CJD Support Network is a UK charity for people with any type of CJD.

Helpline: **01630 673973**
http://www.cjdsupport.net/index.html

Annex C:

Roles and Responsibilities for the reporting, surveillance, diagnosis and care of patients with CJD.

The report in 1996 by the National CJD Surveillance Unit of a new human transmissible spongiform encephalopathy, variant Creutzfeldt-Jakob Disease (vCJD) linked to the epidemic of Bovine Spongiform Encephalopathy (BSE) in cattle, greatly increased the importance of surveillance and research in this whole field.

First, it became apparent that surveillance was necessary not only to track the incidence of the disease and explore its epidemiology but was also vital to the initiation of public health action (for example, in notifying the blood transfusion service about blood donations made by someone with vCJD). Second, the potential scale of the epidemic of vCJD, which still remains uncertain, has created an imperative for high quality research directed at better understanding the molecular basis and pathogenesis of transmissible spongiform encephalopathies; devising a diagnostic test; and developing effective treatments.

We need to ensure a high level of patient referral to the trial whilst maintaining the public health surveillance function, and delivery of the care package for patients with this disease. The Department of Health has asked the Medical Research Council (MRC) to proceed with the PRION-1 initiative to establish a clinical trial infrastructure for investigating quinacrine and other candidate treatments. In addition, the Department has asked the MRC to offer clinical monitoring within the Prion 1 framework to those patients who have chosen to receive pentosan.

Key principles

In order to manage the situation in the United Kingdom well, we must make best use of available clinical resources and knowledge. There are eight key principles that we must follow. These are set out below:

care and support for patients and their families;
skilled clinical investigation to enable a reliable diagnosis to be made;

- early recognition of probable and possible cases of vCJD, sporadic CJD, inherited and other human forms of transmissible spongiform encephalopathy;
- rapid reporting of such cases to the surveillance system;
- prompt gathering of further information from and about patients to allow enhanced surveillance and to identify the need for public health protective action;
- maintenance of rigorous controls to minimise the possible risks of secondary transmission (i.e. person-to-person) via medical procedures or other means;
- quality assuring existing controls on possible primary sources of transmission (e.g. the food chain) and keeping under review the need for new ones;

- high quality research directed at various aspects of human transmissible spongiform encephalopathies (particularly CJD) focussed on achieving early diagnosis and eventual effective treatment for these disorders.

Structures and functions

A number of organisations, teams and committees enable the eight principles to be adhered to and, in this section of the letter, their roles and responsibilities are set out briefly.

a. Departments of Health and other related bodies in England, Scotland, Wales and Northern Ireland

The Departments of Health, as the central government departments with overall responsibility for public health and health services, are responsible for determining policy, allocating resources, co-ordinating implementation and monitoring progress. In these tasks, they are assisted by the Health Protection Agency (a new body, which incorporates the former functions of the Public Health Laboratory Service) and by local arrangements in the devolved administrations. Other expert committees, including the Spongiform Encephalopathy Advisory Committee (SEAC), and agencies including the Medicines and Healthcare Products Regulatory Agency (MHRA) provide advice and support in specialist areas.

b. National CJD Surveillance Unit (NCJDSU) – Lead Consultant: Professor James Ironside

The National CJD Surveillance Unit was established in 1990, and has a high international standing. It is based in the Western General Hospital in Edinburgh and serves the whole of the United Kingdom. The Unit is responsible for monitoring the characteristics of all forms of CJD to identify patterns, trends and risk factors; and, for informing the appropriate body so that prompt, effective action can be taken to protect public health. The National CJD Surveillance Unit has cerebrospinal fluid and genetics laboratories which analyse samples from patients with suspected CJD as an aid to clinical diagnosis. The Unit is responsible for the national pathological surveillance of CJD, involving both histological studies on brain and all other tissues, and protein analysis. The National CJD Surveillance Unit undertakes research on the clinical and diagnostic features of CJD, epidemiology (including the national Case Control Study of risk factors for sporadic and variant CJD, and the investigation of geographically associated cases of CJD), and histopathology and protein analysis of brain and other tissues and fluids. The Unit houses a large bank of brain tissue, cerebrospinal fluid and blood samples which are used for diagnosis and research both within the Unit and with external research groups.

As part of the surveillance activities, staff from the Unit visit each referred patient and their family whenever possible. The Unit provides expert advice, counselling and support for patients with sporadic and variant CJD and their families. The National CJD Surveillance Unit also administers the National Care Package for patients and families with CJD, which co-ordinates care for such patients and their carers throughout the United Kingdom. Staff in the National CJD Surveillance Unit are involved in major programmes of research (much of it in collaboration with other centres in this country

and abroad), and co-ordinate the European CJD Surveillance Network. They also provide advice and expert input to the work of government departments, scientific committees and other organisations and agencies. The Unit is a WHO Collaborative Centre for Reference and Research on the Surveillance and Epidemiology of Human Transmissable Spongiform Encephalopathies.

c. National Prion Clinic – Lead Consultant: Professor John Collinge

The National Prion Clinic at the National Hospital for Neurology and Neurosurgery provides expert clinical advice on diagnosis and management, as well as counselling and support for patients and their families, especially those with, or at risk of, inherited prion disease. The National Prion Clinic has close links with patient organisations. The National Prion Clinic is closely linked with the MRC Prion Unit (see below). Staff at both the MRC Prion Unit and the National Prion Clinic advise governments, other bodies and provide expert input into scientific committees. The National Prion Clinic has a key role in leading and co-ordinating the MRC PRION-I clinical trial, and will provide opportunities for patients to participate in clinical research programmes.

d. Medical Research Council (MRC) Prion Unit

The Medical Research Council (MRC) Prion Unit, based at the Institute of Neurology, Queen Square, London, was established to undertake a major multidisciplinary research programme into human prion diseases, and to translate basic research to clinical practice in the NHS. It has high international standing. It has core research programmes covering molecular genetic studies of human prion disease susceptibility, modes of transmission and their characterisation; clinical research to identify early diagnostic markers and longitudinal studies to establish a cohort for subsequent clinical trials; and, the development of human diagnostic tests and therapeutics. In particular, the MRC Prion Unit in collaboration with the MRC Clinical Trials Unit now has a major role in developing protocols for clinical trials of potential treatments for CJD. The Unit provides laboratory diagnostic services to neurologists and neuropathologists in the UK and overseas, including prion gene analysis and analysis of tonsil and brain biopsies and is a WHO Reference Centre for diagnosis and investigation.

e. Consultants in Communicable Disease Control (CCDCs)

Under existing arrangements for local reporting of CJD, (www.doh.gov.uk/cjd/cjdlocal.htm), neurologists inform their local CCDC of all cases of CJD. CCDCs have a responsibility to investigate each patient's medical history, to report to CJD Incidents Panel, and to advise on infection control measures.

f. CJD Incidents Panel

The CJD Incidents Panel is an expert committee, set up in 2000 by the Chief Medical

Officer in England. Its remit is to assist all bodies responsible for the provision and delivery of healthcare to decide on the most appropriate action to take to handle incidents involving potential transmission of CJD and vCJD between patients through clinical interventions.

g. The CJD Therapy Advisory Group

The Chief Medical Officer in England has also commissioned a group, under the leadership of Sir Michael Rawlins, the Chairman of the National Institute for Clinical Excellence (NICE), to advise on strategic planning of future CJD drug trials. Its main objectives are to maintain an overview of research likely to lead to the development of therapeutics for human disease and identify potential therapeutics for CJD that may be suitable for clinical trial.

h. CJD Tissue Management Steering Committee

This expert committee aims to facilitate human tissue collections on CJD and related diseases and where necessary to help manage access to scarce resources to support research in this area.

In addition to these formal structures, the two patient support groups – the CJD Support Network and the Human BSE Foundation – provide valuable support and advice to families.

Annex D Contact details

The National CJD Surveillance Unit

Enquiries:
Jan.Mackenzie@ed.ac.uk

Clinical Office Telephone: 0131 537 2128
Pathology Telephone: 0131 537 1980 Fax: 0131 343 1404

Address:
National CJD Surveillance Unit
Western General Hospital
Department of Pathology
Crewe Road
Edinburgh
EH4 2XU

Website:
www.cjd.ed.ac.uk/

Director: Professor JW Ironside

The National Prion Clinic

Enquiries:
Phone: 020 3448 4037 Fax: 020 3448 4046 E-mail: help.prion@uclh.org

Address:
National Prion Clinic
Box 98
National Hospital for Neurology & Neurosurgery
Queen Square
London
WC1N 3BG

Website:
http://www.nationalprionclinic.org

Director: Professor John Collinge

The CJD Support Network

Enquiries:
info@cjdsupport.net

Telephone/Fax 01630 673 993

HelpLine/Fax: 01630 673 973

Address: CJD Support Network,
P.O. Box 346
Market Drayton
TF9 4WN

Website:
http://www.cjdsupport.net/

Chairman**: Dr Angus Kennedy**