DA(81)22

DHSS

DEPARTMENT OF HEALTH AND SOCIAL SECURITY

Regional Administrators
Area Administrators
Secretaries to the Boards of Governors
District Administrators

for action

26 November 1981

Dear Administrator

REPORT OF THE ADVISORY GROUP ON THE MANAGEMENT OF PATIENTS WITH SPONGIFORM ENCEPHALOPATHY (CREUTZFELDT-JAKOB DISEASE) (CJD)

1. The Chief Medical Officers of the Health Departments of Great Britain set up a group of experts in 1979 to advise on precautions to be observed when caring for patients suffering from certain neurological diseases thought to be caused by infectious agents in order to avoid any potential hazard from cross-infection from patients or their tissues. This Group have reported to the Chief Medical Officers who have welcomed their report and have decided that it should be published and widely distributed within the Health Service. Five copies of the report are enclosed for Regional Administrators, three for Area Administrators, ten for District Administrators and one for Secretaries of Boards of Governors.

2. Creutzfeldt-Jakob disease is very rare. Apart from a few cases of iatrogenic transmission, no examples of case-to-case transmission or spread of the disease to medical, nursing or laboratory personnel have ever been demonstrated. The report makes a number of practical recommendations on precautions to be observed by all staff involved in the care of these patients: in wards, theatres, laboratories or post-mortem rooms. It is recommended that sufferers should not be accepted either as blood donors or as tissue donors for transplant purposes.

3. The report will be of interest to Regional and Area Medical and Nursing Officers and to Regional Scientific Officers and Blood Transfusion Directors.

4. Some of the recommendations may involve consented changes in the working practices of a number of departments in Districts, and it is therefore recommended that the report be considered by District Management Teams (including District Nursing Officers and District Community Physicians) in order to achieve the necessary degree of co-ordination. In addition, Chairmen of the Medical, Surgical, Pathology and Psychiatric Divisions will wish to draw its conclusions to the attention of their colleagues in their Divisions. The senior Medical Laboratory Scientific Officer in each laboratory in Districts will also need to be aware of its existence.

5. Further copies of the report may be obtained from Her Majesty's Stationery Office, priced £1.

Yours sincerely

Marian Stuart

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ADVISORY GROUP ON THE MANAGEMENT OF PATIENTS WITH SPONGIFORM ENCEPHALOPATHY (CREUTZFELDT-JAKOB DISEASE (CJD))

Report to the Chief Medical Officers of the Department of Health and Social Security, the Scottish Home and Health Department and the Welsh Office

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ADVISORY GROUP ON THE MANAGEMENT OF PATIENTS WITH SPONGIFORM ENCEPHALOPATHY (CREUTZFELDT – JAKOB DISEASE (CJD))

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Dr D A J Tyrrell MD FRS FRCP FRCPath, of the Clinical Research Centre, Northwick Park, Harrow also attended as a representative of the Dangerous Pathogens Advisory Group.

Joint Secretaries (DHSS)

Dr Alison Smithies
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ADVISORY GROUP ON THE MANAGEMENT OF PATIENTS WITH SPONGIFORM ENCEPHALOPATHY (CREUTZFELDT-JAKOB DISEASE (CJD))

REPORT TO THE CHIEF MEDICAL OFFICERS OF THE HEALTH DEPARTMENTS OF GREAT BRITAIN

Introduction

In recent years there has been growing concern amongst health service staff about the possible hazard of cross-infection presented by patients suffering from the spongiform encephalopathy known as Creutzfeldt-Jakob Disease (CJD) and other dementias. It has been suggested that certain of these dementias may be caused by an unconventional transmissible agent or agents. Such agents are sometimes known as "Slow Viruses".

The Departments therefore drew together experts to advise on the problem and a 'Slow Virus Advisory Group' was formed which met 4 times during 1979 and 1980. The Group's terms of reference were:—

> "To consider in the light of available evidence what measures need to be taken by persons caring for and carrying out clinical and laboratory procedures, including post-mortem examinations, on patients with transmissible spongiform encephalopathy or other dementias, in order to avoid any potential hazard from cross-infection by these agents from patients or their tissues."

Background

For some years evidence has accumulated to indicate that the presenile dementia Creutzfeldt-Jakob Disease (CJD) is caused by a transmissible agent. It is estimated that no more than about 20 new cases a year of this rare disease are likely to be identified in the United Kingdom. Transmissibility has been established by injection of brain and other tissues from affected patients into non-human primates and other animals. These injections have often resulted in the development after a year or even longer of a spongiform encephalopathy characteristic of the disease. Iatrogenic patient-to-patient transmission of CJD has been reported to have occurred in 3 cases following neurosurgical procedures and in one following the transplantation of a corneal graft donated by an affected patient. In another report 3 patients, who had all had neurosurgical procedures in one hospital in the same year, subsequently contracted CJD. It is possible that these cases arose as a result of cross-infection during surgery.

Apart from these reports of iatrogenic transmission, there is no convincing evidence of case-to-case transmission of CJD nor of spread of the disease to medical, nursing or laboratory personnel who have come in contact with patients or with nervous or other tissue derived from them. There is no direct evidence for the existence of asymptomatic carriers of CJD although on theoretical grounds their existence is a possibility. It is not known at what stage in the disease it becomes possible for transmission to occur. There is no convincing evidence that dementias other than CJD and kuru (a now fast disappearing condition limited to certain inhabitants of the highlands of New Guinea) are transmissible.

Although Creutzfeldt-Jakob disease has been classified as a slow virus infection the agent causing it behaves quite differently from the viruses associated with slowly progressive cerebral diseases such as the measles virus in sub-acute sclerosing pan-encephalitis (SSPE). For example, unlike SSPE no immune response has been identified in CJD. However, the diagnosis can be made on clinical grounds and can be confirmed by histological examination of brain tissue. The transmissible agent is believed to be similar to the agent associated with scrapie in sheep and most of the properties ascribed to it have been derived by extrapolation from the results of research on the scrapie agent. In particular, a high degree of resistance to the physical and chemical procedures employed for sterilisation and disinfection exists in the scrapie agent and it is assumed that a similar resistance exists in the CJD agent (see Appendix). It is known that the CJD agent in brain tissue has retained its property of infectivity despite prolonged fixation in formalin. Inoculation of tissues from affected patients into non-human primates shows that the brain and nervous tissues are most likely to transmit the disease and that there is a lower risk of infection associated with liver, lung, lymph nodes, kidney and CSF. There is no evidence from the inoculation of material from affected patients into non-human primates that blood, faeces, urine, sputum, tears, sweat and semen are infective. However, the ingestion by monkeys of brain and other tissues taken from an infected chimpanzee has resulted in the passage of the disease, as has the inoculation of blood from infected guinea pigs into other animals.

Diagnosis

A definitive diagnosis of Creutzfeldt-Jakob disease can usually be made on clinical grounds. However, because the disease is very rare most physicians will be unfamiliar with it and it may therefore be misdiagnosed. It may be confused, particularly in its more chronic form, with other neurological and psychiatric disorders. These include Alzheimer's disease, Parkinson's disease and motor-neurone disease. It is important to bear in mind the possibility of CJD in atypical cases and to seek a specialist opinion.

Recommendations

The Advisory Group decided to confine its recommendations to :

Creutzfeldt-Jakob disease

which is the only known transmissible form of spongiform encephalopathy likely to be encountered in Europe.

Although other dementias were included in the terms of reference, earlier claims of possible transmissibility (eg of familial Alzheimer's disease) have not been substantiated and we have concluded that there is insufficient evidence to warrant special precautions in dealing with them.

The Group recommends that the following precautions are observed when attending to patients with known or presumed Creutzfeldt-Jakob disease (referred to as CJD patients in these recommendations). These recommendations are made in the light of present knowledge of the disease, its transmissibility and the properties of the transmissible agent. They will need to be reviewed and, if necessary, amended in the light of future knowledge.

1. Transplant and Tissue Donations

CJD patients should not be accepted as blood donors, and none of their tissues used for transplant purposes.

In the case of corneal grafts the further precaution should be taken that the member of the ophthalmic surgical team responsible for collecting the corneas should be instructed to make specific enquiries to exclude such cases. Corneas should not be taken from demented patients nor from those who die in psychiatric hospitals, nor from patients who die from obscure undiagnosed neurological diseases.

Material from such patients should not be used for the preparation of thromboplastin, growth hormone or other biological extracts used as reagents or for treatment.

2. Ward Procedures

Isolation of CJD patients is unnecessary as the risk of person-to-person cross-infection presented by such patients in the ward is considered to be negligible. However, when procedures are undertaken which carry a risk of contamination with CSF or blood the precautions outlined below should be observed.

The following are examples of such procedures:—

a. lumbar punctures (this includes radiological and other procedures in which CSF is withdrawn)
b. biopsies
c. dressing wounds and bedsores
d. venepuncture and the administration of injections.

The precautions to be observed are:—

i. gloves, aprons, drapes, instruments and other equipment which are disposable should be used
ii. all used equipment should be incinerated.

3. Theatre procedures

a. For surgical procedures on CJD patients not involving brain or spinal cord, and including dental procedures, members of the operating team should wear the following single-use disposable protective clothing:—
   i. Non-wettable operation gowns
   ii. Gloves
   iii. Masks
   iv. Cap
   v. Over-shoes
   vi. A disposable plastics apron under the operation gown
   vii. Suitable eye protection

Disposable drapes and dressings should also be used and should be destroyed after use. Disposable instruments should be used wherever possible. Other instruments should only be used if they can be subjected to the autoclaving

procedures specified in the Appendix. These procedures must be employed before the instruments are re-used.

b. Where the surgical procedure involves the brain (eg cortical biopsy), spinal cord or eye, the following additional precautions should be taken:—

i. The least possible number of persons should take part in the operation.

ii. A one-way flow of instruments should be maintained.

iii. When it is necessary to use instruments not normally regarded as disposable these instruments should under no circumstances be re-used and should be destroyed.

These precautions should also be observed when neurosurgical procedures are carried out on patients in whom the possibility of CJD enters into the differential diagnosis.

4. Transmission of Specimens

Biopsy specimens, specimens of blood and CSF should be placed in the appropriate containers, enclosed in plastic bags and labelled 'Danger of Infection'.

5. Precautions in the Laboratory

Specimens of biopsy material, CSF and blood should be handled with the special precautions recommended in the Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-Mortem Rooms (HMSO £1.75 ISBN 0 11 320464 7).

Formalin-fixed specimens should be regarded as being infective. Special care should therefore be taken to avoid accidental inoculation or other contamination while preparing the tissue for microscopy.

6. Post-mortem examination

The bodies of patients who have died with CJD should not be used for teaching anatomy or pathology. The recommendations made in the Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-Mortem Rooms should be followed when dealing with a known or presumed case of CJD. Disposable equipment should be used whenever possible but if this is impracticable it should be autoclaved as recommended in the Appendix. Special care should be taken by the pathologist and the post-mortem room attendants to avoid any accidental penetration of the skin during the procedure. As few persons as possible should take part in the autopsy or be in the post-mortem room. They should be protected by clothing as specified in Recommendation 3.

7. Accidental Contamination

Accidental injuries or inoculation wounds should be thoroughly washed in running water immediately, and further treatment given as appropriate to the type of injury. An official record must be made of any such accident. It should be emphasised that no case of infection transmitted in this way has ever been recorded.

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APPENDIX

STERILIZATION PROCEDURES

There is evidence that CJD agent will resist standard methods of disinfection and sterilization using heat, formaldehyde, 70% alcohol, ultra violet and ionising radiation. For a number of other methods, eg ether, chloroform and iodophors, there is no evidence either way and we do not recommend their use. Autoclaving infected equipment at 121°C for one hour has been recommended, but experiments have suggested that at least one strain of scrapie agent is resistant to this. Further investigations on sterilization procedures are in progress.

As an interim measure, we recommend that one of the following autoclave procedures should be employed.

i. a single cycle 121° — 124°C (15 lb psi) for 90 minutes holding time at temperature (HTAT)
ii. a single cycle 126° — 129°C (20 lb psi) for 60 minutes HTAT
iii. a single cycle 136° — 138° (30 lb psi) for 18 minutes HTAT or 6 separate cycles 136° — 138°C (30 lb psi) for 3 minutes HTAT

To achieve these cycles, autoclaves should be calibrated by a suitably qualified person.(1) All apparatus should then be washed thoroughly and autoclaved again as necessary.(2)

Limited evidence suggests that exposure to hypochlorite should act as a disinfectant. Therefore, as an interim measure until work in progress provides more reliable information, the use of a 1% dilution of hypochlorite containing 10,000 ppm available chlorine (freshly prepared dilute sodium hypochlorite BP) is recommended for use on contaminated surfaces leaving it for half an hour. For decontamination of laboratory equipment, other than metal (which is corroded by hypochlorites) soaking for 18 hours in a 1% dilution of hypochlorite containing 10,000 ppm available chlorine is advised.(3)

References:

(1) Health Technical Memorandum (HTM)10 — Sterilizers 1980 (HMSO ISBN 0 11 320458 2)
(2) Health Equipment Information (HEI)67 February 1977 11/77 — The Use of Plastics Film, eg Nylon Film, in the Packaging of Items to be Terminally Steam Sterilized.
(3) Health Equipment Information (HEI)88 September 1980 95/80 — Departmental Advice on Some Aspects of Disinfection and Sterilization.
(HEIs are issued by Department of Health and Social Security, Scottish Home and Health Department and Welsh Office).

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DEPARTMENT OF HEALTH AND SOCIAL SECURITY

To: Regional Administrators
District Administrators
Administrators of Special Health Authorities
) for action

6 July 1984

Dear Administrator

MANAGEMENT OF PATIENTS WITH SPONGIFORM ENCEPHALOPATHY (CREUTZFELDT-JAKOB DISEASE (CJD))

1. This letter updates one aspect of the advice given in DA(81)22 on the management of patients with CJD.

2. The Department's Microbiology Advisory Committee has reviewed the Report of the Advisory Group on the Management of Patients with Spongiform Encephalopathy (Creutzfeldt-Jakob Disease (CJD)). As recent research suggests that only the third procedure referred to in the Appendix to the Report (reproduced overleaf) is likely to be effective, the Advisory Committee has recommended that revised advice be issued on sterilisation procedures. This advice is given on an interim basis pending the completion of further research.

3. The revised advice is that the autoclave procedure to be used should be:

a single cycle $134^{\circ}C(^{+4}_{-0})$ (30 lbs psi) for 18 minutes HTAT*;

or

six separate cycles $134^{\circ}C$ $(^{+4}_{-0})$ (30 lbs psi) for 3 minutes HTAT.

4. It is important that all units likely to be affected be made aware of this revised advice. It is therefore recommended that the revised advice be considered by District Management Teams (particularly District Nursing Officers and District Medical Officers). In addition, Chairmen of the Medical, Surgical, Pathology and Psychiatric Divisions will wish to draw the revised advice to the attention of colleagues in their Divisions. The senior Medical Laboratory Scientific Officer in each laboratory in Districts will also need to be aware of it.

5. Copies of the full Report of the Advisory Group on the Management of Patients with Spongiform Encephalopathy can be obtained from Her Majesty's Stationery Office, price £1.

Yours sincerely

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* Hold Time At Temperature

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Appendix J Slow virus infections of the central nervous system

Transmissible encephalopathies or 'slow virus' encephalopathies due to unconventional agents include the human diseases kuru, Creutzfeldt-Jakob disease (CJD) and Gerstmann-Sträussler-Scheinker syndrome (GSS) and, in animals, scrapie in sheep and goats and transmissible encephalopathies of mink, deer and elk. Within the last two years a new animal encephalopathy (bovine spongiform encephalopathy - BSE) sharing some of the characteristics of scrapie has appeared in cattle.

The diseases that affect man are very rare and all of them are known to be caused by agents which do not resemble the more familiar types of virus: also, they are unconventional in that they do not provoke an immune response in the host. One of the major properties of the agents concerned, which is of practical importance, is an apparently remarkable resistance to heat, radiation and chemical inactivation. Experimental work with scrapie as the only available model at the time, but later with CJD, has therefore led to the recommendation of sterilisation and disinfection procedures far more stringent than those usually applied in hospital practice for the control of conventional bacterial, viral and other infectious disease agents. The then DHSS Report of 1981 on the subject of spongiform encephalopathy[1] and the later letter from the Department to administrators (DA(84)16) specified autoclaving contaminated re-usable items at temperatures of 134°C to 138°C for not less than 18 minutes (hold time at temperature) or for six separate cycles of 3 minutes at the same temperature. The ACDP is advised that the downward displacement autoclave, which is the type most commonly used in laboratory work, may be less effective even at these high temperatures than is the surgical steriliser operating with a pulsed vacuum cycle.

Scrapie-infected tissue stored in 10% formalin has been shown to be still capable of transmitting infection to experimental animals, but the application for extended periods of a solution of sodium hypochlorite containing 20 000 ppm available chlorine appears to be effective in at least substantially reducing infectivity when decontaminating surfaces. Some other ostensibly powerful chemical agents such as 10% phenolic disinfectant or even B-propiolactone are regarded as unreliable. Advice should be obtained from specialist sources[2] before any choice is made of alternative disinfectants for decontamination of CJD which must be presumed to have the same level of resistance as that seen with scrapie. There is also a practical difficulty in disinfecting safety cabinets contaminated with unconventional agents because of their resistance to formaldehyde and other fumigants. Special arrangements need to be made in order that filter-changing and maintenance work may be carried out safely.

It has been reported that CJD has been inadvertently transmitted from infected to healthy persons by corneal transplantation, ear drum prostheses made from dura mater, the use of inadequately sterilised neurosurgical instruments and the administration of human growth hormone prepared from the pituitary glands of cadavers. However, these events have been rare and none has occurred since the risk was recognised. While CJD is transmissible it is important to stress that it is not contagious and no proven case of laboratory-acquired infection has been recorded. CJD and GSS are, in any case, rare diseases and kuru is confined to a discrete area of New Guinea where it is in decline. However, the long incubation period of slow virus infections makes

1 DHSS *Advisory Group on the management of patients with spongiform encephalopathy (CJD)*. November 1981 HMSO ISBN 0 11 320778 6.

2 Department of Health, Microbiology Advisory Committee.

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cause and effect somewhat difficult to relate and two recently reported cases[1] of CJD in ex-laboratory workers, who had both handled neural tissues extensively during their working lives, are a matter of concern.

Therefore, particular caution is advised in dealing with tissue from the central nervous system, especially when it comes from known or suspected cases of CJD or GSS. Equipment used in the laboratory and post-mortem room in association with such cases should be subjected to the recommended stringent sterilisation procedures. For this and other reasons, work practices should be reviewed so as to avoid puncture wounds and cuts and the contamination of skin with tissues and body fluids. Eye protection and gloves should be worn.

Following detailed examination of BSE by the Southwood Committee[2] it is clear that at this stage there is insufficient evidence on which to consider the allocation of the agent responsible for this newly emerged encephalopathy to an ACDP hazard group. However, while uncertainty remains about the potential for its transmission to man, it is prudent to treat known or suspected BSE-affected tissues with caution when working with them in the laboratory or animal room. Containment Level 2 precautions with additional measures to guard against puncture wounds and cuts and the contamination of broken skin and eyes are considered to be appropriate. There is no specific information at present on the susceptibility of the BSE agent to heat and chemical disinfectants.

1 Miller D C, Sirwell L et al - two letters in New England Journal of Medicine, 31 March 1988, 318 (No.13) 853-854.

∴ this doc pc 1988

2 Department of Health and Ministry of Agriculture, Fisheries and Food. *Report of the Working Party on Bovine Spongiform Encephalopathy* February 1989 HMSO ISBN 185197 405 9.

post Feb '89.