57752

WHO/EMC/DIS/96.147
Distribution: General
Original: English

F: 57753

Report of a WHO Consultation on Public Health Issues related to Human and Animal Transmissible Spongiform Encephalopathies

With the participation of FAO and OIE

Geneva, Switzerland,
2 - 3 April 1996

WORLD HEALTH ORGANIZATION

Division of Emerging and Other Communicable Diseases Surveillance and Control

Report of a WHO Consultation on Public Health Issues related to Human and Animal Transmissible Spongiform Encephalopathies

With the participation of FAO and OIE

Geneva, Switzerland,
2 - 3 April 1996

WORLD HEALTH ORGANIZATION

Division of Emerging and Other Communicable Diseases Surveillance and Control

TABLE OF CONTENTS

1. INTRODUCTION

During a Consultation on Transmissible Spongiform Encephalopathies (TSEs), which was convened in Geneva on 2-3 April 1996, a group of international experts reviewed the public health issues related to bovine spongiform encephalopathy (BSE) and the emergence of a new variant of Creutzfeldt-Jakob disease (V-CJD) in humans, as officially reported by the United Kingdom on 20 March 1996, and made recommendations for the protection of public health.

The Consultation was opened by Dr H. Nakajima, Director-General of WHO. He stressed the fact that the possible association between BSE and CJD or its variant once again raised concern about the ability of an infectious agent to cross the species barrier between animals and humans, as in the case of salmonella, plague, hantavirus and many other zoonotic diseases.

This Consultation was the fourth organized by WHO on the TSEs since 1991. It reviewed the report of the previous WHO Consultation held on 17-19 May 1995 (document WHO/CDS/VPH/95.145) in the light of recently acquired scientific and clinical findings on BSE and other spongiform encephalopathies, including the newly reported human spongiform encephalopathy.

Drs J. Losos (Canada) and J. Gibbs (USA) were chairpersons of the Consultation and Dr H. Longbottom (Australia) was rapporteur.

2. BOVINE SPONGIFORM ENCEPHALOPATHY

2.1 Background

1. BSE is a transmissible spongiform encephalopathy (TSE)[1] of cattle which was first identified in the United Kingdom in 1986.

   Transmission of BSE to cattle appears to have been via contaminated meat and bone meal in concentrate feed (sheep or cattle may have been the original source of the agent).

   The epidemic in the UK (the only country with a high incidence of the disease) appears to have been due mainly to the recycling of affected bovine material back to cattle before the July 1988 ruminant feed ban became effective.

   To date there is no firm evidence to suggest that either maternal or horizontal transmission occurs. It is noted that no closed herd study has been undertaken to clarify these aspects but a cohort study is under way and will be completed early in 1997.

   The incidence of the disease is declining significantly in the UK, although the measures introduced have not so far brought the epidemic to a halt.

2. The full geographical distribution of BSE is incompletely known. BSE in native cattle has also been identified and reported at a much lower incidence than in the UK in 4 other European countries.

   In these latter countries epidemiological investigations indicate that only some of the BSE cases in native cattle could be proven to be related to consumption of feed which might have been contaminated with the BSE agent.

2.2. Recommendations for the Protection of Public Health

1. No part or product of any animal which has shown signs of a TSE should enter any food chain (human or animal). In particular:

   - All countries must ensure the killing and safe disposal of all parts or products of such animals so that TSE infectivity can not enter any food chain.

   - All countries should review their rendering procedures to ensure that they effectively inactivate TSE agents.

[1] TSE is a term for a group of diseases associated with a transmissible agent, the nature of which is not fully known. The agent displays many virus-like features, such as strain variation and mutation, but differs from conventional viruses in being exceptionally resistant to heat, ultraviolet and ionizing radiation, and to chemical disinfectants.

2. All countries should establish continuous surveillance and compulsory notification for BSE according to the recommendations of the *International Animal Health Code* of the Office International des Epizooties (OIE).

   In the absence of surveillance data the status of a country with respect to the occurrence of BSE must be considered as unknown.

3. Countries should not permit tissues that are likely to contain the BSE agent to enter any food chain (human or animal).

4. All countries should ban the use of ruminant tissues in ruminant feed.

5. With respect to specific products:

   - Milk and milk products, even in countries with a high incidence of BSE, are considered safe. There is evidence from other animal and human spongiform encephalopathies to suggest that milk does not transmit these diseases.

   - Gelatin in the food chain is considered to be safe if produced by a manufacturing process utilizing production conditions which have been demonstrated to significantly inactivate any residual infectivity (selected references: Annex) that may have been present in source tissues.

   - Tallow is likewise considered safe if effective rendering procedures are in place (selected references: Annex).

6. The risk, if any, of exposure to the BSE agent in countries other than UK is considered lower than in UK. Exposure to the BSE agent in UK was likely to be higher prior to the current BSE regulations. More studies are required to allow a full risk assessment. Incomplete risk assessment hinders accurate risk communication and perception.

   The risks at present associated with exposure to the BSE agent from beef and beef products will be minimized if the recommendations of the present group are implemented.

7. Risks from medicinal products and medical devices containing bovine tissues:

   - The importance is reiterated of obtaining bovine materials destined for the pharmaceutical industry only from countries which have a surveillance system in place and which report either no or only sporadic cases of BSE.

   - Removal and inactivation procedures contribute to the reduction of the risk of infection but it must be recognized that the BSE agent is remarkably resistant to physico-chemical procedures which destroy the infectivity of common microorganisms.

   - Measures recommended to national health authorities to minimize the risk of transmitting the agent causing bovine spongiform encephalopathy via medicinal products, in particular parenteral products, which were developed at the WHO Consultation in 1991 (*Bulletin of the World Health Organization*, 1992, **70**: 183-190) continue to be generally applicable.

   - It is recommended that these measures be reviewed and, if necessary, strengthened as more information becomes available.

8. Research on TSE should be promoted, especially regarding rapid diagnosis, agent characterization, and epidemiology of TSEs in humans and animals.

3. A NEW VARIANT OF CREUTZFELDT - JAKOB DISEASE (V-CJD)

3.1. Background

1. TSEs in humans include Creutzfeldt-Jakob disease (CJD) (which may occur in sporadic, inherited, and iatrogenic forms), Gerstmann-Sträussler-Scheinker syndrome and fatal familial insomnia (both of which are inherited disorders), and Kuru, a disorder which was associated with ritualistic cannibalism in Papua New Guinea.

A newly recognized variant form of CJD (**V-CJD**) has been identified in 10 patients in the UK. In contrast to typical cases of sporadic CJD, this variant form has affected young patients (mean age, 26.3 years) with a relatively long duration of illness (mean, 14.1 months).

The characteristic neuropathological profile in this variant consists of numerous widespread Kuru-type amyloid plaques with surrounding vacuolation and severe cerebellar lesions. No abnormalities in the prion protein gene have been demonstrated so far in any of the cases.

2. **Case definition for V-CJD.** To date, all patients identified in the UK who died of the disease were 41 years of age or less.

   A suspect case shows the following clinical features:

   - A psychiatric presentation with anxiety, depression, withdrawal and other behavioural changes with progression to neurological abnormalities.
   - Onset of a progressive cerebellar syndrome within weeks or months of presentation.
   - Forgetfulness and other memory impairment, with dementia in the late stages.
   - Myoclonus in the late stages.

   The EEG does not show the changes normally observed in classical CJD.

   Less common features include early onset of dysaesthesia in limbs and face at presentation, and chorea, extrapyramidal and pyramidal signs later in the illness.

Neuropathological diagnosis is mandatory for confirmation of suspected **V-CJD** cases.

Confirmatory examination of the brain should show the following neuropathological features:

- Numerous widespread Kuru-type amyloid plaques surrounded by vacuoles.
- Spongiform change most evident in the basal ganglia and thalamus.
- Prion protein accumulation in high density shown by immunocyto-chemistry, particularly in the cerebellum.

3.2. Conclusions

1. **V-CJD** is reported at present only in the UK; its geographical distribution needs to be better defined.

2. A link has not yet been proven between **V-CJD** in the UK and the effect of exposure to the BSE agent.

   The most likely hypothesis for **V-CJD** is the exposure of the UK population to BSE; further data are urgently required from scientific studies on these variant cases. More retrospective and prospective monitoring and surveillance studies on all forms of CJD, modelled on current European collaborative studies, are required throughout the world.

LIST OF PARTICIPANTS

Dr Annick **Alperovitch**, Director of the INSERM Research Unit, "Recherche épidemiologique en neurologie et psychopathologie", Unité INSERM 360, Hôpital de la Salpetrière, 75651 Paris Cedex 13, France

Dr R. **Bradley**, Private Consultant, BSE Coordinator, Central Veterinary Laboratory, Ministry of Agriculture, Fisheries and Food, New Haw, Addlestone, Surrey Kl5 3NB, UK

Professor Dr H. **Diringer**, Head, Section: "Unconventional Virus Diseases", Robert Koch Institut, Bundesinstitut für Infektionskrankheiten und nicht übertragbare Krankheiten, Nordufer 20, D-13353 Berlin, Germany

Dr D. **Dormont**, Direction des Sciences du Vivant, Departement de Recherche Médicale, Service de Neurologie, Centre d'Etudes Nucléaires (CEA), BP 6, 92265 Fontenay-aux-Roses, France (unable to attend)

Dr D. C. **Gajdusek**, Chief, Laboratory of Central Nervous System Studies, National Institute of Neurological and Communicative Disorders and Strokes, National Institutes of Health, Bethesda, Maryland 20892, USA (unable to attend)

Dr J. **Gibbs**, National Institute of Neurological and Communicative Disorders and Strokes, National Institutes of Health, Bethesda, Maryland 20892, USA **(Co-Chairman)**

Dr F. **Horaud**, Département de Virologie, Institut Pasteur, 75724 Paris Cedex 15, France

Dr J. W. **Ironside**, Senior Lecturer in Pathology, Honorary Consultant in Neuropathology, National Creutzfeldt-Jakob Disease Surveillance Unit, Department of Clinical Neurosciences, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK

Dr Helen **Longbottom**, Director, Surveillance and Epidemiology Section, AIDS/Communicable Diseases Branch (MDP15), Commonwealth Department of Health and Family Services, BPO Box 9848, Canberra ACT 2601, Australia **(Rapporteur)**

Dr J. **Losos**, Director-General, Laboratory Centre for Disease Control, Tunney's Pasture, Ottawa, Ontario KIA OL2, Canada **(Chairman)**

Professor J. R. **Pattison**, University College, London Medical School, Chairman of the Spongiform Encephalopathy Advisory Committee, Administration: Gower Street, London WCIE 6BI, UK

Dr L. **Schonberger**, Assistant Director for Public Health, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA

Professor P. **Smith**, Head, Department of Epidemiology and Population Sciences, London School of Hygiene and Tropical Medicine, Keppel Street, London WCIE 7HT, UK

Professor Dr A. **Somogyi**, Director, Federal Institute for Health Protection of Consumers and Veterinary Medicine, Thielallee 88-92, 14191 Berlin, Germany

Professor M. **Vandevelde**, Institute of Neurology, Veterinary Faculty, University of Berne, Innerberg Str. 40A, CH-3044 Innerberg, Switzerland

Dr C. **Weissmann**, University of Zurich, Department of Molecular Biology I, ETH-Hönggerberg, PF 1, 8093 Zurich, Switzerland (unable to attend)

Other Organizations

Food and Agriculture Organization of the United Nations (FAO)
Dr Y. Cheneau, Chef du Service de Santé Animale, Division de la Production et de la Santé Animale, Via delle Terme di Caracalla, I-00100 Rome, Italy

Dr P. Roeder, Animal Health Officer, Infectious Disease Emergencies, Animal Health Service, Via delle Terme di Caracalla, I-00100 Rome, Italy

Office international des Epizooties (OIE)
Dr R. Reichard, Head, Scientific and Technical Department, 12, rue de Prony, 75017 Paris Cedex, France

European Commission
Dr A. J. Wilson, Head of Veterinary Public Health Section, Veterinary Legislation Unit, European Commission, 84 Rue de la Loi, 1040 Brussels, Belgium

Professor P. Peters, National Expert, Public Health Analysis, Policy and Programme Coordination, Development and Evaluation Unit, DGV/ F/I, Public Health, European Commission, JMO, L-2920 Luxembourg

Observers

Austria
Professor H. Budka, University Professor of Neuropathology, University of Vienna, Institute of Neurology, AKH, POB48, A-1097 Wien

France
Dr T. Baron, Head, Virology Unit, CNEVA Lyon, 31 Avenue Tony-Garnier, BP 7033, F-69342 Lyon Cedex 07

Dr Isabelle Capek, Médecin inspecteur de Santé publique, Ministère du Travail et des Affaires sociales, Direction Générale de la Santé, 4 Passage de l'Espérance, F-94000 Créteil

Ireland
Dr E. Weavers, Senior Research Officer, Department of Agriculture and Food Ireland, Veterinary Research Laboratory, Dublin 15

Ms B. Cannon, First Secretary, Permanent Mission of Ireland to the United Nations Office and to the Specialized Agencies at Geneva, 1211 Geneva 2, Switzerland

Mr D. Denham, Permanent Mission of Ireland to the United Nations Office and to the Specialized Agencies at Geneva, 1211 Geneva 2, Switzerland

Dr J. Devlin, Deputy Chief Medical Officer, Department of Health, Hawkins House, Dublin 2

Italy
Dr M. d'Alessandro, Neurologist, Laboratory of Virology, Istituto Superiore di Sanità, Viale Regina Elena, 299, 00161 Rome

Japan
Dr Y. Kaji, Deputy Director, Division of Veterinary Sanitation, Bureau of Environmental Health, Ministry of Health and Welfare, Tokyo

Dr T. Kurata, Director, Department of Pathology, The National Institute of Health, Toyama 1-23-1, Shinjuku-ku, Tokyo 162

Dr E. Sanatani, First Secretary, Permanent Mission of Japan, 3 Chemin des Fins, Case postale 337, 1211 Geneva 19, Switzerland

New Zealand
Mr C. Feek, Chief Medical Adviser, Ministry of Health, P.O. Box 5013, Wellington

Russian Federation
Dr L. Malychev, Counsellor of the Permanent Mission of the Russian Federation to the United Nations Office and other International Organizations at Geneva, Case postale, 1211 Geneva 20, Switzerland

Switzerland
Monsieur G.-O. Segond, Président du conseil d'Etat, Chargé du Département de l'Action sociale et de la Santé, République et Canton de Genève, Rue de l'Hôtel-de-Ville, Geneva (unable to attend)

Dr B. Hörnlimann, Swiss TSE Coordinator, Swiss Public Health Office, Section for Epidemiology and Infectious Diseases, 3097 Liebefeld/Bern

United Kingdom of Great Britain and Northern Ireland
Dr Ailsa Wight, Senior Medical Officer, Department of Health, Room 546B, Skipton House, 80 London Road, London SE1 6LW

Dr Lena Robinson, Senior Medical Officer, Department of Health, Room 546B, Skipton House, 80 London Road, London SE1 6LW

USA
Dr B. W. J. Mahy, Director, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333

Dr T. Gomez, Veterinary Epidemiologist, US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Centers for Disease Control and Prevention, Atlanta, GA 30333

Dr K. Bernard, Health Attaché, United States Mission to the United Nations Office and other International Organizations at Geneva, 11 Route de Pregny, 1292 Chambésy, Switzerland

Dr Clara Witt, PHS Veterinary Consultant, US Mission, 11 Route de Pregny, 1292 Chambésy, Switzerland

Secretariat

Dr H. Nakajima, Director-General, World Health Organization, Geneva

Dr Hu Ching-Li, Assistant Director-General, World Health Organization, Geneva

Dr D. L. Heymann, Director, Division of Emerging and other Communicable Diseases Surveillance and Control, World Health Organization, Geneva

Dr F.-X. Meslin, Disease Surveillance and Control, Division of Emerging and other Communicable Diseases Surveillance and Control, World Health Organization, Geneva **(Secretary)**

Dr L. J. Martinez, Division of Emerging and other Communicable Diseases Surveillance and Control, World Health Organization, Geneva

Dr K. Stöhr, Disease Surveillance and Control, Division of Emerging and other Communicable Diseases Surveillance and Control, World Health Organization, Geneva

Dr G. A. Clugston, A/Director, Division of Food and Nutrition, World Health Organization, Geneva

Dr E. Griffiths, Chief, Biologicals, Division of Drug Management and Policies, World Health Organization, Geneva

Dr F. Käferstein, Chief, and Dr S. Miyagawa, Food Safety, Division of Food and Nutrition, World Health Organization, Geneva

Programme on Mental Health, Division of Mental Health and Prevention of Substance Abuse, World Health Organization, Geneva (Dr C. Bolis, Dr A. Janca, and Dr J. Orley)

Dr M. Kaplan, Member of WHO Expert Advisory Panel on Zoonoses, 23 Chemin de Marly, 1245 Collonge, Geneva

EMC Professional Staff (Dr J.-C. Alary, Dr O. Cosivi, Dr J. LeDuc, Dr M.C. Thuriaux, Dr E. Tikhomirov)

WHO Regional Office for the Americas
Dr S. Corber, Director, Division of Disease Prevention and Control, Pan American Health Organization, World Health Organization, 525 23rd Street, NW, Washington, D.C. 20037, USA

WHO Regional Office for the Eastern Mediterranean
Dr M. H. Wahdan, Assistant Regional Director, P.O. Box 1517, Alexandria 21511, Egypt

WHO Regional Office for Europe
Dr G. Klein, Director, Environment and Health, WHO/EURO, Scherfigsvej 8, Copenhagen, Denmark
Dr C. A. Van der Heyden, Assistant Director, WHO EURO Department of Environmental Health, and Director, WHO European Centre for Environment and Health, Bilthoven Division, Juliana plain 7, 3708 BH Zeist, Netherlands

ANNEX

Brown, P., Rohwer, R.G. & Gajdusek, D.C. (1986). Newer data on the inactivation of scrapie virus or Creutzfeldt-Jakob disease virus in brain tissue. Journal of Infectious Diseases, 153: 1145-1148.

Di Martino, A., Safar, J., Ceroni, M. & Gibbs, C.J. jun. (1992). Purification of non-infectious ganglioside preparations from scrapie-infected brain tissue. Archives of Virology 124: 111-121.

Diringer, H. & Kimberlin, R.H. (1983). Infectious scrapie agent is not as small as recent claims suggest. Bioscience Reports 3: 563-568.

Hunter, G.D. & Millson, G.C. (1964). Studies on the heat stability and chromatographic behaviour of the scrapie agent. Journal of General Microbiology, 37: 251-258.

Hunter, G.D. (1965). Progress toward the isolation and characterisation of the scrapie agent. In: Slow, Latent and Temperate Virus Infections. Edited by D.C. Gajdusek, C.J. Gibbs, jun. & M. Alpers. NINDB Monograph No. 2. pp. 259-262. U.S. Government Printing Office, Washington, D.C.

Kimberlin, R.H., Millson, G.C. & Hunter, G.D. (1971). An experimental examination of the scrapie agent in cell membrane mixtures. III. Studies of the operational size of the scrapie agent. Journal of Comparative Pathology, 81: 383-391.

Marsh, R.F. & Hanson, R.P. (1969). Physical and chemical properties of the transmissible mink encephalopathy agent. Journal of Virology, 3: 176-180.

Millson, G.C., Hunter, G.D. & Kimberlin, R.H. (1976). The physio-chemical nature of the scrapie agent. In: Slow Virus Diseases of Animals and Man. Edited by R.H. Kimberlin, ch. II, pp. 243-266, North-Holland, Amsterdam.

Pocchiari, M., Macchi, G., Peano, S. & Conz, A. (1988). Can potential hazard of Creutzfeldt-Jakob disease infectivity be reduced in the production of human growth hormone? Inactivation experiments with the 263K strain of scrapie. Archives of Virology, 98: 131-135.

Pocchiari, M., Peano, S., Gonz, A., Eshkol, A., Maillard, F., Brown, P., Gibbs, C.J. jun., Xi, Y.G., Tenham-Fisher, E. & Macchi, G. (1991). Combination ultrafiltration and 6M urea treatment of human growth hormone effectively minimizes risk from potential Creutzfeldt-Jakob disease virus contamination. Hormone Research, 35: 161-166.

Taguchi, F., Tamai, Y., Uchida, K., Kitajima, R., Kojima, H., Kawaguchi, T., Ohtani, Y. & Miura, S. (1991). Proposal for a procedure for complete inactivation of the Creutzfeldt-Jakob disease agent. Archives of Virology, 119: 297-301.

Tamai, Y., Taguchi, F. & Miura, S. (1988). Inactivation of the Creutzfeldt-Jakob disease agent. Annals of Neurology, 24: 466-467.

Taylor, D.M., Dickinson, A.G., Fraser, H., Robertson, P.A., Salacinski, P.R. & Lowry, P.J. (1985). Preparation of growth hormone free from contamination with unconventional slow viruses. Lancet ii, 260-262.

Taylor, D.M., Fraser, H., McConnell, L., Brown, D.A., Brown, K.L., Lamza, K.A., Smith, G.R.A. (1994). Decontamination studies with the agents of bovine spongiform encephalopathy and scrapie. Archives of Virology, 139: 313-326.