

MEDICAL RESEARCH COUNCIL

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CJD WG 78/7

WORKING GROUP ON CREUTZFELDT-JAKOB DISEASE

Minutes of meeting held on Friday 6 October 1978 at 20 Park Crescent London W1N 4AL

Present: Professor J.N. Walton (Chairman), Dr. A.M. Adelstein, Mr. K. Burns (ARC Observer), Professor C.O. Carter, Professor W.B. Matthews, Mr. P. Smith, Dr. A. Smithies (Health Departments' Observer), Professor B.E. Tomlinson, Professor M.P. Vessey.

Headquarters staff: Dr. Katherine Levy, Dr. Victoria Harrison, Miss Roberta Withnall.

1. Chairman's opening remarks

The Chairman opened the meeting by reminding members that the Working Group had been set up by the Neurosciences Board following their consideration of the report of the meeting on 9 March, to make arrangements, where possible, for implementation of the recommendations then made for carrying out epidemiological studies on Creutzfeldt-Jakob (C-J) disease. While acknowledging their importance it was not the task of the Working Group to consider the problems of isolation, characterisation, distribution in the body, routes of infection or methods of destruction of the C-J agent: committees set up by the Health Departments and the ARC were considering the need for further studies in these areas.

2. Confirmation of proposed terms of reference (CJD WG 78/2)

The Chairman referred the meeting to the proposed terms of reference:

- i) To consider the practicalities of implementing the recommendations made at the meeting on 9 March 1978 on the feasibility of carrying out epidemiological studies on Creutzfeldt-Jakob disease.
- ii) To co-ordinate action as appropriate.
- iii) To report to the Neurosciences Board annually, making at least an informal report at some stage in the 1978/79 session.

Members agreed that the proposed terms of reference were unexceptionable and they were confirmed without amendment.

3. Consideration of arrangements to be made to implement the recommendations made at the meeting on 9 March 1978 (CJD WG 78/3)

a) Retrospective analyses

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- i) After some discussion it was agreed that it would be worthwhile to compare Professor Matthews' data on histologically proven cases, with the data which could be provided by the OPCS. The comparison of data from the two sources would, in addition to indicating whether or not any particular occupations or any clusterings were involved, provide some idea of the accuracy of the recording of death from C-J disease by death certificate.

It was noted that a detailed study of C-J disease was being undertaken in France under the auspices of the NIH. In view however of national variations in the incidence of disease it was accepted that it would be worthwhile to carry out a similar study in the UK.

- ii) The Chairman suggested that Professor Matthews' Department in Oxford would be the obvious place for the studies to be undertaken. Professor Matthews kindly agreed that - subject to the availability of space - the study could be based in his department, under the supervision of himself, Professor Vessey, and Mr. Smith.
- iii) It was agreed that the first priority in embarking on the analyses was for firm diagnostic criteria to be established.
- iv) Considering the OPCS data provided by Dr. Adelstein on deaths in England and Wales in 1975 (CJD WG 78/4), it was suggested that OPCS should be asked to provide the name, address, place of death and occupation for deaths listed under the following ICD categories: 339.9, 290.1, 347.9, 331.9 and 348. A one year scan in the first instance might be adequate for the latter category: if no cases of C-J were revealed, further scans would not be required. A ten year scan would probably be appropriate for the other categories. A one year scan of deaths due to senile dementia might also be considered. It was agreed that exact details of the scans required and the years to be covered should be decided by Professor Matthews, in consultation with Professor Vessey, Mr. Smith and Dr. Adelstein. It was further agreed that deaths due to ischaemic cerebrovascular disease (437) and other types of arteriosclerosis need not be examined.
- v) It was agreed that it would be necessary to follow up further any cases recorded by Professor Matthews which were not identified in the OPCS data, and that if the OPCS data identified other cases, confirmation of diagnoses would be required in these instances.
- vi) Professor Vessey raised the question of how complete ascertainment needed to be: Mr. Smith said that, with regard to clustering, a positive finding with incomplete ascertainment would need to be treated with caution, but that a negative finding might be significant.
- vii) It was pointed out that as the OPCS data covered England and Wales only, similar information for Scotland should be sought from the appropriate Scottish office, to boost numbers. The office undertook to look into this.
- viii) It was pointed out that if occupational histories from relatives were to be taken, the necessity of including a control group in the study would have to be considered. It was agreed that the need for a control group, and if so the nature of the group which would be required, would be discussed by Professor Matthews, Professor Vessey and Mr. Smith in the light of the results of the analysis of data.
- ix) Professor Vessey suggested that the plan of investigation should be to examine occupations recorded on death certificates in the categories specified over a ten year period and to compare these data with controls. If having done this there was no suggestion of an occupation association, it would not then be worth looking for clustering, interviewing relatives or confirming diagnoses.
- x) Professor Vessey confirmed that Sir Richard Doll had agreed to look at the information available from the study of 34,000 doctors on the medical register in 1953 to ascertain whether any deaths from C-J disease had been recorded. It was noted that it would be of particular interest if more than one death had occurred from the disease as this would be in excess of the incidence expected in a population of this number. It was emphasised however that information on occupation, by speciality, available in 1953 was likely to be rather crude.

xi) Medical laboratory technicians were another occupational group possibly worthy of study. Dr. Adelstein mentioned coal miners and steel workers as groups on which there is likely to be data which could provide negative information.

b) Prospective studies

- i) The Working Group agreed that it would also be worthwhile to carry out prospective studies on this disease.
- ii) As a first requirement it would again be necessary to have clearly defined diagnostic criteria. The need for histological verification of the diagnosis should also be considered.
- iii) The necessity for a long time scale for the study was accepted, and it was agreed that the actual period should be determined in the light of the results from the retrospective studies.
- iv) With regard to the identification of patients it was considered that the most effective means would be to write to every neurologist in the UK. It was likely that few if any cases would not be seen by a neurologist, but a statement might also be placed in the medical press, and letters sent to the appropriate professional associations representing psychiatrists and psychogeriatricians seeking information on relevant cases. OPCS should also be asked to provide notification of all death certificates received which mention C-J and those other disease categories to be covered.
- v) Questionnaires, for interviewing relatives, might ask for information on previous illnesses and whether the patient had been a blood donor, as well as on occupational history.
- vi) The recommendation for immunological/genetic studies was discussed. It was agreed that determination of HLA status would be of value, and that each specimen should be examined in two laboratories, perhaps referring it to the tissue typing laboratory nearest to the patient, and to a second laboratory, in Oxford or London, which would type all specimens. In view of the slender evidence for the involvement of a genetic factor it was suggested that general genetic screening would not at this stage be profitable. It was considered that an immunologist should be consulted about this aspect - particularly on whether complement, rather than enzyme polymorphisms, should be examined. It was also agreed that the storage of serum samples should be arranged. Professor Carter advised that the setting up of a family study might be considered.

4. Conclusions and recommendations

It was concluded that, while it was possible that no new findings would emerge from the proposed studies, the Working Group shared the view of the Neurosciences Board that efforts should be made to launch a UK study on the epidemiology of C-J disease. It was therefore recommended that funds, in the form of a special project grant, should be made available to Professor Matthews, for the employment of a scientific assistant (who would organise and co-ordinate the study on a day-to-day basis), for secretarial assistance, running costs and travelling expenses. Dr. Levy agreed that Professor Matthews could proceed immediately to seek a suitable scientific assistant. Additional funds would be required to obtain data from OPCS, and the appropriate Scottish office, for Mr. Smith to look for clustering and for examination of the Doll/Hill data. Professor Matthews, Professor Vessey and Mr. Smith agreed to collaborate in the preparation of detailed proposals (which would include diagnostic criteria and protocols for

both the retrospective and prospective studies) if possible by mid-November. These proposals should be circulated by the office to all members of the Working Group for approval.

5. Timetable and arrangements for future meetings

It was agreed that it would not be necessary to hold a meeting until possibly the spring of 1979: a date would therefore be arranged nearer that time.

6. Any other business

None.