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MEMORANDUM

TO: Dr. J.M. Payne

27th June, 1978.

FROM: Dr. R.H. Kimberlin

Proposal to initiate work on Creutzfeldt-Jakob disease at MRE Porton

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Introduction

On June 1st, 1978, the Wildy Committee unanimously approved the proposal that the initial experiments on Creutzfeldt-Jakob disease should be set up at the Microbiological Research Establishment, Porton, where facilities for the safe handling of CJ infected animals already exist. The urgent need to begin these long term studies would justify the inconvenience and expense (see later) of holding animals at Porton while similar facilities were being built at Compton.

Objectives

The purpose of these experiments is to make some comparison between CJ and scrapie agents using the techniques already developed for identifying different strains of scrapie agent. One technique involves a quantitative assessment of the severity and distribution of lesions in anatomically defined areas of brain. This method is applicable to mice and hamsters because the behaviour of different strains of scrapie agent has been extensively studied in these two species. The other main technique involves measurement of incubation period in mice of different genotypes to study the interaction between strains of CJ agent and the mouse gene sinc. This work can only be done in mice.

Experimental Plan

The initial requirement is to transmit a number of different sources of CJ agent to mice and hamsters. However, at least one successful transmission of CJ to mice has already been reported by Dr. E.E. Manuelidis and it is hoped to begin strain typing of this isolate immediately, if Dr. Manuelidis agrees. The first experiments will therefore be carried out with the following groups of inocula:-

1. 6 different samples of human CJ brain - confirmed by expert neuropathologists.

2. 2 samples of normal human brain.

3. 2 groups of environment controls injected with saline only.

4. 1 sample of mouse passaged CJ from Dr. Manuelidis.

This gives a total of 11 inocula. Each one will be injected into groups of mice and hamsters as follows:-

A. 20 inbred BSC mice (sinc ^{s7}) kept in 4 boxes.

B. 20 inbred IM mice (sinc ^{p7}) kept in 4 boxes.

C. 10 outbred golden hamsters kept in 10 boxes.

Small colonies of BSC and IM mice will be supplied by Dr. A.G. Dickinson and bred at Porton to give these numbers for the experiment. Mice of either sex will be used. Female outbred golden hamsters will be purchased from a local supplier.

Isolation Facilities

The animal experiments will be carried out entirely within a room in the toxic animal wing at MRE Porton. This room will contain a few marmosets and some mice injected with CJ by Dr. R.N.P. Sutton. The room is fitted with a suitable safety cabinet to be used for the preparation of inocula and injection of animals. These procedures will be carried out by myself under the supervision of experienced Porton staff. In the early stages of the work, clinical diagnosis and post mortem removal of tissues (using the safety cabinet) will be performed by Compton staff: myself and Miss C.A. Walker with the help of Mr. G.C. Mills when required. The difficulties of interpreting clinical signs in ageing mice will necessitate frequent visits to Porton. Later, the staff at Porton will take over some of these tasks as they become experienced.

Compton staff who work in the toxic animal wing at Porton will comply with the safety requirements. These include showering into the unit, a complete change of clothing into the boots, gowns, gloves and hats provided and showering out of the unit. Staff will also receive the standard series of vaccinations required for all those working in the unit.

It is expected that the experiment will run for about 2 years, the lifespan of the animals. The only materials to leave the unit will be frozen tissue for passage studies and formalin fixed brain for histological studies. Frozen tissue will be kept at Porton until such time as it can be moved to a similar unit at Compton. Formalin fixed tissues will be taken out of the Porton unit, at intervals, in "Porton bins" and accompanied to Dr. H. Fraser's laboratory in Edinburgh. Dr. Fraser will perform the histological studies.

Expenditure

The experiment will be conducted in collaboration with Dr. H. Fraser, who is preparing a separate estimate for the provision of facilities for histology. The main costs of the animal work fall under thee headings.

1. Animals The estimated cost of the experiment in the first year is as follows:-

Labour including overheads	£1445
Food & bedding	500
Space usage	155
Total amount payable to M.R.E. Porton	£2095 + VAT
Cost of hamsters	£ 150

2. Travel and subsistence (1st year) Many visits will be made at short notice and at weekends. Therefore the estimate is based on the use of a private car, 6 times a month with a return journey of about 100 miles, and on subsistence for 2 people, away for more than 5 but less than 10 hours.

Travel	£ 886
Subsistence	£ 173

3. Laboratory supplies Instruments and disposable items such as syringes, gloves, gowns etc.

£ 150

It is difficult to estimate costs in the second year, as these will depend on results obtained in the previous year. However, it is unlikely that travel costs will change much but the animal costs could increase by 50%.

R.H. KIMBERLIN.