Conference report

Journal of Medical Genetics 1987, **24**, 572-573

The First European Symposium on Neurofibromatosis

The first European Symposium on Neurofibromatosis (NF) was sponsored by LINK, the British neurofibromatosis patients' association, and held over three days at the Runnymede Hotel, Egham, Surrey. The meeting was divided into two parts; the first was a scientific workshop devoted to laboratory studies of NF. This was attended not only by those actively working on NF but also by scientists working in related fields whose expertise brought fresh insights into ways of approaching NF research. Many of the scientists stayed on for the second part of the symposium, an open clinical meeting, and the clinical/scientific interaction which resulted was particularly fruitful.

The scientific programme was divided into four main topics: the cellular phenotype and the cellular genotype of Von Recklinghausen neurofibromatosis (VRNF), growth control, and a session on bilateral acoustic neurofibromatosis (BANF). In the session on cellular phenotype, Peltonen (Turku) and Krone (Ulm) presented an overview of their previously reported work on the cellular constituents and cytogenetic studies of neurofibroma tissue respectively. As abnormal Schwann cell proliferation appears to be one of the key factors in the development of neurofibromas; in the session on growth control a series of five papers (given by Edgar, Planegg-Martinsried; Schachner, Heidelberg; Mirsky, London; Bunge and Porter, St Louis) reviewed what is known about the development of normal Schwann cells and their interaction with the neuronal axon. These papers stimulated lively discussion as to what could be the trigger for the development of neurofibromas, and in particular several possible 'candidate genes' were suggested which had not yet been used in linkage studies.

The session on cellular genotype began with a series of short papers from groups working on VRNF linkage (Darby, Stanford; Huson, Harrow; Skolnick, Utah; Seizinger, Boston; Mulvihill, Washington; Ponder, London). The majority of results were clearly negative with only two markers giving slightly positive lod scores. Several of the markers had been studied by a number of different groups and it was obvious that there was a clear

need for future collaboration, to pool existing data and to avoid unnecessary repetition. Under the chairmanship of Professor Marcus Pembrey, a further 'round table' discussion was held to address this problem. This resulted in the formation of a consortium of those working on VRNF linkage, the first task of which was to produce an exclusion map as presented in this edition of the journal. A mechanism was also agreed which will ensure regular pooling of further data and which will also ensure the rapid confirmation or rejection of promising but unconfirmed linkage results, while preserving the credit for those who made the first observation, if it is confirmed. This presents a major step forward in minimising the present waste of effort in the competitive lucky dip of linkage studies.

The scientific session concluded with the presentation of their work on BANF by Martuza and Seizinger (Boston). Their original work on acoustic neuromas has now been extended with more tumours from patients with BANF. These tumours have shown consistent allele loss of chromosome 22 markers when compared with lymphocyte DNA, suggesting that the gene responsible for the development of acoustic neuromas is on 22q and that the mechanism is similar to that responsible for retinoblastoma and Wilms' tumours. Linkage studies of chromosome 22 markers in BANF families are now in progress. These markers have already been studied in VRNF families and the results from several groups are all consistently negative.

The programme for the clinical meeting reflected the wide variety of specialists involved in the management of VRNF patients. Its aim was to inform the audience, drawn from an equally wide range of specialities, about the incidence and modes of presentation of the various disease complications, and the treatments available.

The session opened with two overviews of VRNF based on the findings of population studies: the recent South Wales study (Huson, Harrow) and the 39 year follow up of the patients originally identified by the study of Borberg (Mulvihill, Bethesda). The pathology of VRNF was then reviewed by Lantos (London), followed by Riccardi (Houston), who

presented theories of pathogenesis and possible approaches to treatment. As neurofibromas are replete with mast cells and their development and growth is often associated with itching, he has assessed the use of the mast cell stabiliser ketotifen in controlling the pruritus and also the growth of large neurofibromas. The drug has only been used in a small number of patients but has been successful in controlling the pruritus; the results of growth control, however, were less conclusive.

A session on genetic counselling (Baraitser, London) followed. The difficulties in helping families come to terms with the uncertainties of long term prognosis and the cosmetic disfigurement caused by the disease were highlighted. Dr Baraitser was then joined by two LINK members who gave their personal experience of VRNF. Both had been frustrated by the lack of information about the disease and the numerous clinic visits to different specialists which were not coordinated. They felt that there was a clear need for other countries to follow the American example and establish neurofibromatosis clinics so that the patient always has one doctor taking an overview of the disease. Many VRNF sufferers do not receive genetic counselling and therefore are unprepared when their children develop complications when they had been told VRNF was just a 'skin problem'.

The programme then moved on to review the experience of different specialists in managing the complications of VRNF. These were: mental handicap and psychiatry (Samuelsson, Gothenburg), neurology (Hughes, London), oncology (Westbury, London), ophthalmology (Taylor, London), and plastic surgery (Poole, Oxford).

The only other form of NF reviewed at the meeting was BANF (Martuza, Boston). He drew attention to the often subtle skin manifestations of this form of neurofibromatosis. Some of the skin neurofibromas in BANF may have a different gross morphology from those in VRNF. These 'BANF plaques' are usually slightly raised skin plaques with

an irregular surface, often with darker or more prominent hair, yet on biopsy they are indistinguishable from other neurofibromas. Martuza also stressed that the diagnosis of BANF should be considered in any patient presenting with an acoustic neuroma before the age of 30 years, in any child with a meningioma or Schwann cell tumour, and in persons with only a few café au lait spots or neurofibromas and no Lisch nodules. Surgery on acoustic neuromas in BANF is difficult, yet if an early diagnosis is made and the tumours are therefore small at the time of surgery, preservation of facial nerve function and some degree of hearing is possible with modern techniques.

The classification of the different forms of NF arose several times during the meeting. It was generally felt that VRNF, BANF, and segmental neurofibromatosis can be clinically distinguished as distinct entities. There are, however, a number of patients who have been previously reported or are at present under review who appear not to fall into these categories but who clearly have a form of NF. If these patients are evaluated in a standardised manner worldwide, then further subclassification should become possible. The pitfalls of confusing the different types of NF and 'lumping' them together as one disease were also mentioned both in terms of genetic counselling and management.

The success of this meeting and its excellent organisation were a great credit to LINK. The plans for future international collaboration in all aspects of NF, and in particular linkage studies of VRNF, would not have come to fruition without it. The scientists and clinicians involved in this endeavour are grateful to the association for making this possible.

SUSAN M HUSON
*Division of Inherited Metabolic Diseases,
 Clinical Research Centre,
 Watford Road, Harrow,
 Middlesex HA1 3UJ*