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HEREDITARY DISEASES PROGRAMME
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REPORT OF A
 JOINT WHO/NATIONAL NEUROFIBROMATOSIS FOUNDATION MEETING
 ON THE CONTROL OF NEUROFIBROMATOSIS:
 NATIONAL/INTERNATIONAL MANAGEMENT

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1. Introduction

Neurofibromatosis (NF) is a serious, genetically determined neurological disorder that affects both sexes and all races and ethnic groups. There are at least two forms of neurofibromatosis: NF1, which is commoner (affecting 1 in 4 000 births) and can affect the ectodermal, mesodermal, and neural tube systems; and NF2 (affecting 1 in 100 000 births), which appears only to affect tissues in the ectodermal system.

The following is a summary of discussions and recommendations made by the participants.

2. Educational Materials

Leaflets covering the clinical, genetic, and management aspects of NF1 and NF2, which are available as educational materials to the general public, were reviewed at the meeting; the majority were written in English. Selected texts are also available in Dutch, French, and Spanish upon request from NNFF. Although the information in each brochure was similar, the participants agreed that slight modifications should be made to adapt to the local health care structures in different countries. It would be helpful if a selection of brochures could be made available to those countries in the process of developing lay organizations for the condition and setting up NF clinics for the first time, so that they could design specific leaflets best-suited to their own needs.

3. Resources Available for the Management of NF

There is no uniform pattern of organizing health care for NF patients and the participants at the meeting had themselves been responsible for setting up NF clinics because of their own personal interest.

A consensus for the management of patients with NF1 was issued by the National Institutes of Health in 1987. It was agreed at the meeting that affected individuals should undergo annual medical reviews to determine whether they have any symptoms or signs of complications. Bearing in mind the age of the patient, the examining physician should estimate the extent of any complications that may present, e.g., learning difficulties in school-age children. Whether or not an investigation is required to screen for complications is equivocal. A few centres recommend routine cranial imaging to monitor the development of optic gliomas, while most believe that the very low frequency of symptomatic optic gliomas and lack of proven evidence as to the benefit of detecting presymptomatic lesions does not justify this approach.

Under the auspices of WHO it may be possible to target key clinicians in different countries to encourage them to develop a service for the care of NF patients. Clinicians with an interest in developing expertise in NF could be encouraged by the provision of international visiting fellowships which could be sponsored by lay organizations.

When it is decided to set up an NF clinic, it would be useful if the organizers inform the International Neurofibromatosis Association (INFA), which would provide an information package to facilitate the establishment of the planned clinic. Such an information package could include the National Institutes of Health Consensus Statements on NF and Acoustic Neuroma, a variety of non-technical leaflets, copies of reports from WHO meetings, and an invitation to become a contributing centre to the NNF International Database.

The NNF International Database is now in operation and any NF centre can contribute to it. The collection of standardized data that are thus produced was applauded at the meeting and it was suggested that information gathered by the database in certain key areas could be highlighted for future study; for example, learning disabilities, the natural history of optic glioma, and the natural history of plexiform neurofibromatosis, with particular respect to their predilection for malignant degeneration.

4. Opportunities for International Research Collaboration

The longest-running research collaboration in the world is the NNF International Consortium on Gene Function in NF1 and NF2, which is managed by the NNF in the USA. The consortium, which meets approximately every nine months, includes all the major laboratories in the world that are currently working on NF1 and NF2. Its purpose is for scientists to share new data regularly and thus to accelerate the pace of progress in NF research.

The NNF recently formed the international NF1 Genetic Analysis Consortium, with both clinicians and molecular biologists represented. The aim of the consortium is to encourage laboratories to submit clinical data on all patients identified as having mutations within the NF1 gene. In this way, it is hoped to identify genotype/phenotype correlations.

Treatment for specific complications is particularly relevant to NF1. There is still controversy as to the ideal approach to investigating and managing certain aspects of NF1, such as learning disabilities, presymptomatic detection and treatment of optic gliomas, and the identification of patients at risk for developing malignant nerve tumours. In contrast, the investigations used for assessing and treating patients with NF2 are much more uniform. However, since this condition is much rarer, it is important that liaison between centres is encouraged so that new developments in management can be compared for large numbers of patients.

International research collaboration on these issues could be further encouraged by convening workshops/symposia of experts to consider specifically such matters. Funding for such meetings would need to be provided by the lay NF organizations, but the INFA could play a coordinating role.

Although no curative treatment is yet available for any of the disease manifestations of NF1 or NF2, it is likely that further understanding of the function of the disease genes may lead to preventative treatments. These would need to be assessed in well-organized trials, and a number of centres would need to collaborate to ensure maximum participation.

How such treatments could be quantitatively measured could be the subject for discussion within the framework of a workshop in the near future.

5. Conclusions and Recommendations

The NNFF, together with the INFA, and WHO should collaborate on the issues outlined below.

- Available literature on NF1 and NF2 for the general public should be compiled for review by the NNFF and the INFA so that the most appropriate information on every aspect of the two disorders can be assembled for distribution to centres starting up new NF clinics as well as to individuals setting up new lay organizations.
- Clinicians in different countries should be encouraged to develop an expertise in neurofibromatosis. An information package should be made available to such individuals and the opportunities should be created for visiting fellowships to enable them to attend recognized NF clinics.
- International research collaboration on the molecular genetics of NF is well established and encouraged by the regular meetings of the NNFF International Consortium on Gene Function in NF1 and NF2. The recently formed International NF1 Genetic Analysis Consortium is a move towards international collaboration at the clinical level, but there are specific aspects of both NF1 and NF2 where such collaboration could be further encouraged.
- Future joint meetings of the NNFF and/or the INFA and WHO should be encouraged; these could be convened as satellite meetings at either major international genetics or neurofibromatosis meetings.

6. List of Participants

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