Preface

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Diabetes is one of the most serious challenges to healthcare worldwide and is projected to affect 239 million people by the year 2010, a doubling in the prevalence since 1994. The incidence of insulin-dependent diabetes is also increasing in children, who will therefore be prone to late complications of diabetes, since long duration of disease is known to increase the incidence of complications. Furthermore, the life expectancy of people with insulin-dependent diabetes is reduced by approximately 5–10 years compared with people without diabetes. Thus, diabetes has a significant economic impact on society, both in terms of healthcare resources and lost productivity in the workplace. Diabetes is the most common cause of progressive and disabling neuropathy in the world. A significant breakthrough in the treatment and/or management of diabetic peripheral neuropathy (DPN), therefore, represents a unique opportunity to reduce the burden to society and, more importantly, to improve the quality of life of people with diabetes.

The most common type of DPN is a distal symmetrical sensory polyneuropathy (DSSP). All types of nerve fibres are involved in DSSP, but the small myelinated and unmyelinated fibres can be predominantly affected. In diabetic small-fibre polyneuropathy, the main manifestations include a fibre-length-dependent sensory loss affecting temperature and pinprick sensations. However, there is relative preservation of light touch, proprioception, tendon reflexes and muscle strength. In addition, patients will manifest more or less severe, sometimes life-threatening, autonomic disturbances. In such cases, examination of nerve biopsy specimens reveals a selective or predomi-

nant loss of small myelinated and unmyelinated axons. Eventually, all classes of nerve fibres are affected and lost in distal nerves.

Although the aetiopathology of DPN is probably multifactorial, recent research may have discovered a potential new breakthrough in the treatment of this disease. The neurotrophic factor, nerve growth factor (NGF) has been shown to promote survival, differentiation and maintenance of small-fibre sensory and sympathetic neurons in the peripheral nervous system. This new drug provides an exciting possibility for a putative therapy for this complication of diabetes. Indeed, encouraging results from studies with NGF in animal models of neuropathy have suggested that NGF may ameliorate peripheral nerve degeneration. The cloning of the human gene for NGF and the subsequent synthesis of recombinant human NGF (rhNGF) have enabled extensive preclinical and clinical studies to be performed. Preliminary phase I and II trials with rhNGF, the first neurotrophin to be evaluated in clinical trials, have shown it to be both efficacious and safe in human diabetic subjects. Promising results from the phase II trial have prompted confirmation of the efficacy of rhNGF in the treatment of neuropathy in phase III multicentre studies and these are underway. The evaluation of efficacy is an extremely demanding task requiring the quantification of the endpoints, and the development of new methods for the assessment of sensory deficits.

This symposium explored the rationale for rhNGF as a putative treatment for DSSP. An international faculty of experts in the field of diabetes and its complications, from

both clinical and research perspectives, reviewed the pathology of DPN, their long-term consequences, the cost of the disease and the different methods used for the evaluation of neuropathy in diabetic patients, both in clinical practice and in clinical trials. The preclinical and clinical data (phase I and phase II) supporting rhNGF as a potential treatment for the disease were also reviewed. The success of rhNGF in DPN should encourage the investigation of its effects in other disabling neuropathies that are characterised by small-fibre lesions, such as familial amyloid polyneuropathy and the late-onset sensory neuropathy observed in AIDS.

This first symposium on rhNGF, held in June 1998 at the 8th Meeting of the European Neurological Society in Nice, France, generated a lot of enthusiasm and interest in rhNGF as a novel putative agent for the treatment of DPN and also potentially the first of a new class of therapeutic agents. It was a great pleasure for us to chair the symposium and to discuss rhNGF in DPN with diabetologists and neurologists. We look forward to the next meeting on rhNGF and to meet again the experts who made this meeting a great success. In conclusion, all that remains to be said is that rhNGF represents a molecule with great potential in an area of unmet clinical need.