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Dear Reader,

It has been more than a quarter of a century since Professor Péter Kempler published the first Hungarian summary of the pathophysiology and the diagnostic and therapeutic possibilities of neuropathies. Over the past 25 years, there have been tremendous advances in our knowledge about neuropathies, but unfortunately, in many ways, this has not been matched by changes in clinical practice. A significant portion of patients are not even diagnosed, and the treatment they receive is not in line with current guidelines. This is why this summary is so important, as it can help clinicians both in making a diagnosis and in initiating state-of-the-art therapies.

The book is also a reminder that neuropathy is a truly multidisciplinary disease. Although the medical community considers diabetes to be its main cause, there are many other common diseases that may also be responsible. To name just the most prominent, alcoholic and non-alcoholic liver disease, chronic renal failure, hypertension, various nutritional deficiencies, and metabolic disorders can lead to peripheral nerve damage. This goes to show that there is almost no field of medicine that does not have to deal with the issue of neuropathy. A thorough knowledge of the disease is also extremely important because the typical clinical symptoms—described in detail in this monograph—can be recognised by simple examinations, which means a diagnosis can be made even in the GP's office and, on the basis of this knowledge, effective treatment can be started. Early diagnosis is also a prerequisite for preventing serious complications in neuropathies. Compared to the previous three monographs, perhaps the greatest novelty of this work is the presentation of data from Hungary based on domestic studies and an evidence-based approach to the management of neuropathy based on large-scale clinical trials. Clinical trials have now shown that the combined administration of conventional treatment options (benfotiamine, alpha-lipoic acid) in appropriate doses, supplemented by symptomatic treatment, can effectively improve clinical symptoms and the risk of long-term complications in advanced neuropathies.

I am particularly pleased that the most prominent members of the profession, including current and former colleagues of the Department of Internal Medicine and Oncology (formerly known as the 1st Department of Internal Medicine), have made significant contributions to the production of this excellent monograph—this is no coincidence, as a significant number of Hungarian neuropathology specialists started their careers in the working group led by Professor Péter Kempler.

I am confident that fellow medical experts who read this book will be able to use the latest theoretical knowledge to diagnose and effectively treat neuropathies in their daily practice. The importance of this step cannot be overstated in the case of such a substantial, under-diagnosed and now well-treatable disease.

I highly recommend this book to all interested experts, and I wish you success in applying the knowledge gained in your daily work.

Budapest, 10 December 2024

Dr István Takács
Professor of Medicine

Introduction

What you hold in your hands is the fourth manual on neuropathies. The first book was published in 1996, the second in 2002, and the third in 2011. The longest period between two publications was before this, the current edition, and I pondered for a long time whether I should even bother. Similarly to this edition, all three previous editions were also published in English and the third in Russian as well, just as the fourth edition will be published in both languages.

When we started our neuropathy studies at the 1st Department of Internal Medicine at Semmelweis University, this complication was considered an interesting but rare disease; it was thought not to occur in type 2 diabetics. In 1981, 44 years ago, my boss at the time, András Várdi, gave me a short Lancet article on cardiovascular autonomic neuropathy in diabetic patients. It was written by David Ewing — it is based on his description that we still refer to tests for autonomic neuropathy as Ewing tests. András told me that although I was still young, I had to do some scientific work, for which I would need only an ECG and a blood pressure monitor. This would allow me to examine 10-12 patients if I was lucky and then possibly even give a lecture on the subject. To this day, I am very grateful to András. Unfortunately, he is no longer with us due to an unfortunate accident.

Carrying out cardiovascular reflex tests is a simple but time-consuming task and, as a young trainee, I didn't have the opportunity during my day-to-day work. At the same time, I was well aware of the potential of research within the framework of the medical students' scientific association (TDK). By then, the Department was headed by Professor Holló, who agreed to take on four TDK students, although he noted that he was not aware that I had done any scientific work. I was very lucky to have these four bright, hardworking third-year students who did an excellent job for four years. I would like to highlight the work done by Anna Mosonyi and Andrea Tumpek. Based on the positive initial experience, 88 TDK students are still working in the working group today. Ten of them have been admitted to the faculty and five of them have defended their doctoral theses.

Work on neuropathy typically either addresses the neurological damage caused by diabetes or follows a neurological line of thought. The authors of this book are predominantly internists, though distinguished experts in neurology, paediatrics, and psychiatry have also participated in writing this book. At the same time, we have tried to address the main concerns of general practitioners, internists, and diabetologists in particular. A separate chapter covers aspects of paediatric diabetes and the characteristics of neuropathy associated with pre-diabetes. In addition to diabetes, the characteristics of neuropathy associated to chronic liver disease, chronic kidney disease, and haematological diseases are described in detail. Compared to the third edition, a new chapter has been added, including several new diagnostic methods, sections on polycystic ovary syndrome and thyroid disorders, and sections on critical illness neuropathy, depression, and neuropathy.

Several new diagnostic techniques not included in previous editions are presented, including ultrasound examination of the nerves, punch skin biopsy, and corneal confocal microscopy.

The presentation of the risk factors for neuropathy and the different treatment options for neuropathy is now more comprehensive. Within the former, the importance of vitamin D should be highlighted.

The list of authors has expanded along with the content. In total, 56 authors have contributed to the fourth edition. I am grateful for the help of those who contributed to the writing of the first edition, many of whom have become prominent authorities and professors in the field over the decades. I was very happy that the staff of the 2nd Department of Internal Medicine and Centre for Nephrology and Diabetology of the Clinical Centre of the University of Pécs, the Department of Medicine of the University of Szeged, and the School of Internal Medicine of the University of Debrecen also participated in the preparation of the fourth edition, and I would like to thank them all for their work. I am particularly honoured that many staff members from my workplace, the Department of Internal Medicine and Oncology of Semmelweis University (formerly known as the 1st Department of Internal Medicine), have contributed to the writing of the book chapters; some of them my own staff members, some of them members of other working groups.

The first three editions of the neuropathy handbook were authored entirely by Hungarians. For the fourth edition, the authorship has been internationalised, with leading international authorities on neuropathic diabetics who have been working on neuropathy for decades, each contributing a new chapter, and several of them chairing the Neuropathy Working Group of the European Diabetes Association (NEURODIAB).

I would also like to thank my wife, Dr Éva Kádár, for her help in so many ways, and Dr Tamás Várkonyi for his work as co-editor.

Dr Péter Kempfer

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