

UIU HATIEGANU UNIVERSITY OF MEDICINE AND PHARMACY CLUJ-NAPOCA ROMANIA



## IULIU HATIEGANU" UNIVERSITY OF MEDICINE AND PHARMACY **DOCTORAL SCHOOL NEUROSCIENCE** PROGRAM

2022-2023 | M2.5.2

9 MAY, 2023 VIRTUAL MEETINC



### PhD NEUROSCIENCE PROGRAM COORDINATOR



#### Dafin F. Mureşanu

President of the European Federation of NeuroRehabilitation Societies (EFNR)

Secretary General AMN (Academy for Multidisciplinary Neurotraumatology)

Past President of the Romanian Society of Neurology

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### INTERNATIONAL GUEST LECTURER



#### Wolfgang Grisold

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### **COURSE PROGRAM**

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#### 9 MAY, 2023

VIRTUAL MEETING

- 12:00 12:25 Wolfgang Grisold /Austria Neuropathic pain – frequency, diagnosis and treatment
- 12:25 13:00 Wolfgang Grisold /Austria Electrophysiology, Ultrasound or both?
- 13:00 13:20 Wolfgang Grisold /Austria Paraneoplastic neuropathies



### INTERNATIONAL GUEST LECTURER



#### WOLFGANG GRISOLD AUSTRIA

Prof. Wolfgang Grisold is a specialist for neurology and psychiatry. From1989 until 2016, he has been heading the department of neurology of the KFJ hospital in Vienna, Austria.

His special interests apart from general neurology are neuromuscular disease and neurooncology, palliative care and education in neurology. His has particular expertise in neuromuscular disease in regards to clinical findings, electrophysiology, neuropathology and imaging. He has participated in 2 EU projects on paraneoplastic syndromes, and in 2 ECCO- EU projects on oncologic video education. His focus in the past years was the effect of cancer on the peripheral nervous system.

He currently published 600 publications among them 4 books (Atlas of neuromuscular disease, 2 editions) and has presently 225 Pubmed quoted publications, 330 Abstracts and presented over 1400 lectures.

He has been involved in education from the aspects of CME and CPD (EFNS, UEMS, WFN), residency training (Austrian society of neurology and UEMS), board examinations (Austrian society and UEMS/EBN), patient and caregiver education and European and international department visits (UEMS/WFN). He has chaired the education committee of the EFNS from 2002 until 2007, has been the co-chair of the education committee of the WFN, where he also chaired the teaching course committee until 2015.

From 2000 to 2002, he was the founding president of the Austrian Society of Neurology. He is presently the secretary general of the WFN from 2013 and is involved in educational projects as the WFN Teaching centers and WFN department visits.

He was president of the UEMS/EBN (past president), and the EANO (European Association of neurooncology). Within ECCO he chairs the ACOE (accreditation body for CME) and is a member of the UEMS EACCME CME governance board.

In Vienna he is a member of the KAV ethics committee and also a member of the higher medical council of the city of Vienna.

He also works in a private neurology office in Vienna, where combines clinical work with neuromuscular disease and electrophysiology.



#### DAFIN F. MUREȘANU Romania

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, President of the European Federation of Neurorehabilitation Societies (EFNR), Chairman Communication Committee of the European Academy of Neurology (EAN), Past President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), Chairman "RoNeuro" Institute for Neurological Research and Diagnostic, Corresponding Member of the Romanian Academy, Member of the Academy of Medical Sciences, Romania and secretary of its Cluj Branch. He is member of 17 scientific international societies (being Member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 10 national ones, being part of the executive board of most of these societies. Professor Dafin F. Muresanu is also a specialist in Leadership and Management of Research and Health Care Systems (specialization in "Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998"; "MBA - Master of Business Administration - Health Care Systems Management, The Danube University - Krems, Austria, 2003"). He has performed valuable scientific research in high interest fields such as: neurobiology of central nervous system (CNS) lesion mechanisms; neurobiology of neuroprotection and neuroregeneration of CNS; the role of the Blood-brain barrier (BBB) in CNS diseases; developing comorbidities in animal models to be used in testing therapeutic paradigms; nanoparticles neurotoxicity upon CNS; the role of nanoparticles in enhancing the transportation of pharmacological therapeutic agents through the BBB; cerebral vascular diseases; neurodegenerative pathology; traumatic brain injury; neurorehabilitation of the central and peripheral nervous system; clarifying and thoroughgoing study on the classic concepts of Neurotrophicity, Neuroprotection, Neuroplasticity and Neurogenesis by bringing up the Endogenous Defense Activity (EDA) concept, as a continuous nonlinear process, that integrates the four aforementioned concepts, in a biological inseparable manner.

Professor Dafin F. Muresanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation Summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary Neurotraumatology (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 500 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (260 papers indexed on Web of Science-ISI, H-index: 25) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: "Dimitrie Cantemir" Medal of the Academy of The Republic of Moldova in 2018, Ana Aslan Award 2018 -"Performance in the study of active aging and neuroscience", for the contribution to the development of Romanian medicine, National Order "Faithful Service" awarded by the President of Romania in 2017; "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, Faculty of Medicine, the "Iuliu Hatieganu Great Award 2016" for the best educational project in the last five years; the Academy of Romanian Scientists, "Carol Davila Award for Medical Sciences / 2011", for the contribution to the Neurosurgery book "Tratat de Neurochirurgie" (vol.2), Editura Medicala, Bucuresti, 2011; the Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.



### ABSTRACTS

#### **NEUROPATHIC PAIN- FREQUENCY, DIAGNOSIS AND TREATMENT**

#### WOLFGANG GRISOLD

Per definition neuropathic pain is pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system. This definition by the ISAP is very broad and allows a wide range of differential diagnostic considerations. The precise frequency of neuropathic pain is unknown. In particular, as the pain syndrome is often mixed pain, and needs differentiation from nociceptive, visceral and sometimes psychologic causes. Commonly a distinction is made between peripheral and central neuropathic pain syndromes.

Examples for peripheral neuropathic pain syndromes are neuropathies, nerve compression, herpes zoster and several neuralgic syndromes in the cranial nerves. Central causes are post stroke pain, some cases of multiple sclerosis, and also phantom pain. Deafferentation pain is observed in extensive nerve lesions, and must be differentiated from nociceptive pain. Pruritus in some cases can be an equivalent to neuropathic pain.

The causes for neuropathic pain syndromes are numerous and range from a focal lesion, towards infection, immune mechanisms, malignancy and several others. Often despite extensive investigations, a definite lesion can not be found. Pain is a subjective experience, and despite many scores and evaluations, relies on the patients subjective experience.

Based on the anatomical structure of peripheral nerves, the examiner is able to distinguish not only between an axonal and demyelinating lesion, but also find clues for ganglionopathies. Increasingly the focus shifts to nodopathies, diseases of the ion channels, and also the wide field of small fiber neuropathy.

The role of neurology on the treatment of cancer pain is growing, and an accurate distinction between direct and indirect effects of cancer therapy, as well as side effects of therapy must be made with accuracy.

The therapy of neuropathic pain is predominately based on drugs, which are anticonvulsants and antidepressants and surface agents. Also opiates need to be considered in the therapeutic concepts. In addition, many other therapies often based on physiotherapy and local interventions are used, which have a variable grade of evidence. Patients also often turn to alternative and complementary medicine. Treatment of patients with neuropathic pain can be difficult, and the dose and management of specific therapies need careful explanations and instructions.

The role of neurology in identifying neuropathic pain syndromes is important and is often part of an interdisciplinary setting.

#### PARANEOPLASTIC NEUROPATHIES

#### WOLFGANG GRISOLD

The diagnostic criteria published by the PNS (Paraneoplastic Neurological Syndromes) Euronetwork in 2004 provided a useful classification of PNS, and included central and peripheral manifestations.

For neuropathies subacute sensory neuronopathy (SSN) was the most frequently observed entity, whereas other types of neuropathies as pure sensory neuropathy, sensorimotor neuropathy, demyelinating neuropathies, autonomic neuropathies, and focal nerve or plexus lesions, were less frequent.

At the time of publication the focus was on onconeural antibodies, which was expanded by newly described antibodies in due course.

Knowledge regarding the mechanisms of PNS has since increased.

Neuronal surface antibodies emerged later, as well as similarities between the side effects of immune check point inhibitors and PNS were described in the past years.

In addition to several frequently observed solid tumors found in association with PNS also interest on the mechanisms underlying the neuropathies observed in lymphoma, paraproteinemias, and multiple myeloma has increased.

In a smaller number the spectrum of paraneoplastic neuropathies has added motor neuropathies, small fiber neuropathies as well as autonomic and nerve hyperexcitability syndromes. In addition, also focal neuropathies, as cranial nerves, plexopathies, and mononeuropathies, are considered in some cases to be of paraneoplastic origin, although the level of evidence is often low.

The differential diagnosis for paraneoplastic neuropathy, during the course of cancer disease is mainly chemotherapy-induced peripheral neuropathy (CIPN) among other rarer types of nerve involvement in cancer.

Therapeutic options are often restricted to symptomatic interventions, mostly directed against pain and disability. Exceptions could be immune mediated demyelinating neuropathies which receive treatment schemes resembling their non paraneoplastic manifestations.

The awareness for paraneoplastic neuropathies, their characteristics and 'their tumor associations are important in clinical practice.

Important links:

Arch Neurol 2010 Mar;67(3):330-5. doi: 10.1001/archneurol.2009.341.

Neurooncol Pract. 2015 Dec;2(4):167-178. doi: 10.1093/nop/npv025.

Front Neurol 2021 Oct 1;12:706169. doi: 10.3389/fneur.2021.706169.

Front Neurol 2021 Oct 1;12:706169. doi: 10.3389/fneur.2021.706169.

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### NEUROMUSCULAR DISEASES IN PRACTICE: ELECTROPHYSIOLOGY, ULTRASOUND OR BOTH ?

#### WOLFGANG GRISOLD

The knowledge on neuromuscular diseases has expanded in past years based on genetic, immunologic and other specific developments. In addition also new therapies not only for immune mediated, but also genetic diseases appear.

Electrophysiology and increasingly ultrasound, remain standard investigations in the assessment of the peripheral nervous system. As an example for peripheral nerves the basic electrophysiological distinction between axonal and demyelinating neuropathies allows a gross differentiation in regard to etiology. As an additional example conduction block can signal a local problem of can be specific for a disease.

The standard investigation for the neuromuscular system is electrophysiology, mainly based on nerve conduction studies (NCV) and electromyography (EMG). This is a good approach to diagnose neuropathies, myopathies and also local entrapment sites of peripheral nerves. Methods of neurophysiological investigation are available in large numbers, allow detailed diagnostics and can be considered the gold standard.

The advent of imaging techniques (as CT, MR and ultrasound among others) has allowed to observe the morphology of muscle and nerve adding new dimensions. MR techniques can be used for nerve and muscle pathology and also the detection of metabolic changes in some cases.

Ultrasound, as an imaging technique not only visualizes morphology, but also adds the real time observation of movements, as muscle contraction, fasciculations, and in entrapment sites also the movement and gliding of peripheral nerves. It can also be of importance when there is need to investigate the whole length of a nerve, in search for additional lesions, and local or general changes in nerve diameter, vascularization and finally also to investigate continuity. However despite the increasing high resolution of US, the depth of US investigation is limited to the surface of the body, and proximal nerves can often not be sufficiently reached and CT and MR must be used.

Less frequently used in neurology, are interventions as anesthesia, infiltrations, BTX therapy under US guidance in the neuromuscular system. Much experience has been gathered in local pain interventions by anesthesiology and post surgical pain care.

In clinical practice electrophysiology and US methods are synergistic and not only increase the accuracy of neuromuscular testing, also allow to add additional morphological features, which can not be directly observed in electrophysiology. However, ultrasound imaging is unable to asses the functional properties of nerves (sensory ,motor and autonomic fibers ), and in the EMG of muscles specific electrophysiological properties as de - and reinnervation as examples.

Representative cases studies investigating a cranial nerve, the brachial plexus, an individual nerve, a case of generalized neuropathy and a muscle will be presented and examined with both methods and the pros- and cons- will be discussed.

The lecture aims to describe the application of both methods, electrophysiology and ultrasound, based on their technical attributes, in standard conditions.

