

## STATEMENT

*By Prof. Dr. Stefka Yancheva, MD, PhD*

*External Member of Academic Jury of University Multidisciplinary Hospital for Active Treatment and Emergency Medicine „N. I. Pirogov“*

*Regarding Dr. Maria Ivanova Dimitrova, MD*

In accordance with Art. 60, paragraph 2, of the Regulations for the development of the academic staff at UMHAT “N. I. Pirogov”, according to the decision of the Academic Jury with protocol №HC-02-21/28.04.2021 and Order №RD-26 - 1166/05.05.2021 of the Executive Director of UMHAT “N. I. Pirogov” I have been chosen as a member of an Academic Jury with the task to present a **statement**.

**Regarding:** Competition for the academic position of "Associate Professor" in the scientific specialty "Neurology", announced in the State newspaper, issue 19/05.03.2021.

The only candidate participating in the competition is Dr. Maria Ivanova Dimitrova - Head of department “Neurology” at UMHAT “N.I. Pirogov”.

### **Biographical data. Education. Professional development. Qualifications and specializations.**

Doctor Maria Dimitrova, MD has graduated from the Mathematical High School “Baba Tonka” Rousse in 2001. She received a master’s degree in Medicine at Medical University – Sofia (MU), Bulgaria in 2007. She acquired a specialty in “Neurology” at Military Medical Academy in 2013. In the period 2013 - 2018 she has been a resident and assistant at the Clinic of Nervous Diseases at the Military Medical Academy. In 2018 she defended a dissertation for the degree of Doctor of Medicine. In 2018 she obtained a master's degree in Health management at MU, Sofia - Faculty of Public Health. Since 2018 she is the Head of the “Neurology” department at UMHAT “N. I. Pirogov”. She has been certified neurosonologist since 2014. She has repeatedly participated in national and foreign training courses.

**Research activity. Main contributions.** Dr Dimitrova, MD participates in the competition with 79 scientific papers and reports. There is included a dissertation for the degree of "Doctor of

Medicine" / I / and an independent monograph, which in the text I will indicate with a capital letter M. She is the first author in 34 of her scientific publications.

**The scientific publications of Dr. Dimitrova, MD are in the following areas:** Obstructive Sleep Apnea (OSA), Multiple Sclerosis (MS), Cerebrovascular diseases (CD); Spinal pathology (SP), Neuro-psychological research in neurologic diseases, COVID-19, and others.

**Obstructive Sleep Apnea (OSA).** Doctor Dimitrova has defended a dissertation /I/ on the subject of “Neuropsychological disturbances in OSA” for the degree Doctor of medicine. She has the largest number of academic publications for “OSA” /III 5, 6, 10, 14, 21; IV. 1.4., 4.2.4, 2.5, 4.2.7, 4.2.9, 4.2.10, 4.2.11/. In recent years “OSA” is considered an important medico-social problem. Early diagnosis of the disease and early implementation of adequate treatment are of great importance for the prevention of severe complications. Dr. Dimitrova has not only discovered the most important anthropometric predictors for “OSA” but proves the positive correlation with the severity of the disease. /I; IV 4.2.7/. Obesity, the obsolescence of “OSA” and the presence of comorbid diseases are not only the main risk factors /RF/ for the occurrence of cognitive disorders but are also important for their severity. The candidate determines the specificity of the methods for assessment of cognitive deficit and creates an easily applicable short battery for its research; /I; V 4.1.4, 4.2.11 /. Dr. Dimitrova, MD determines the specifics of the cognitive and personality profile of patients with OSA - disorders of psychomotor speed and executive functions. The study of the psychological aspects of the disease /anxiety, depression, fatigue/ establishes other pathological changes and their connection with comorbid diseases / I; IV 4.1.18, 4.2.10 /. The use of visual rating scales with CT and MRI of CNS proves the presence of global or regional cortex atrophy and their link to certain spheres of the cognitive dysfunction. The severity of global cortex atrophy correlates with the minimum oxygen saturation and the age of the patients /I/. *The dissertation and academic publications and reports regarding „OSA” have academically theoretical and practical contributions.*

**Multiple Sclerosis.** The disease has great medical and social importance. MS remains one of the main reasons for lasting disability and death in young age groups. Doctor Dimitrova MD has dedicated many academic publications for the modern, pathogenetically reasoned MS therapies. She discusses the criteria for the inclusion of interferons as a resource for modeling the course of

the disease. She describes in detail the indications and side effects from the administration of Dimethyl Fumarate and Ocrelizumat /III 18,24,35/. The disability of the patients is aggravated by the presence of some non-motor symptoms / disorders in cognition, behavior, emotions, mood, etc./. Dr Dimitrova M.D presents scales widely used in clinical practice for their assessment. /III 9,31;IV 4.2.1/. In a review article, she discusses the therapeutic options for opticomyelitis and presents the results of immunoglobulin treatment in a patient unresponsive to corticosteroids (III 23). *The publications have scientific and practical contribution.*

**Cerebrovascular diseases (CVD).** Dr Dimitrova M.D has dedicated her own monograph to the problems of CVD. "*Diagnostic and therapeutic approaches for Cryptogenic Brain Infarction*", Sofia, 2021 /M/ and a lot of academic publications and reports. In my opinion, I believe that every chapter of the monograph should be considered a publication, as it contains a bibliographical reference.

*The monograph* is dedicated to an incredibly important medico-social problem. Acute cerebrovascular disorders (ACDs) are characterized by high mortality, and stroke survivors are often left with severe neurological and cognitive deficits. It is alarming that 10% to 20% of strokes occur between the ages of 18 and 54. The positive effect from applying the modern therapeutic methods for ACVI depend on the early diagnosis. Despite the use of highly informative diagnostic methods, between 30 and 40 percent of cerebral infarctions are considered cryptogenic /TOAST, 2015/. This prevents the conduction of adequate individualized treatment of patients. Therefore, the publication of this monograph by Dr. Dimitrova, MD, deserves admiration. After the epidemiology and classification of cerebral infarctions, she describes the definition of a cryptogenic cerebral infarction. The diagnostic process for patients with unknown reasons for stroke is well observed with an algorithm created by M. Serhal and R. Mendrichaga /2019/. After the initial assessment, patients undergo ultrasound, neuroimaging, biochemical, genetic, and other testing. Among them, cardiac research occupies a significant place. Changes in the brain parenchyma and cerebral circulation are examined by CT,MRI, MRTA, and if necessary - by conventional angiography.

The cardiogenic sources of embolism are reviewed in detail. Along with the more trivial ones, the possibilities for embolic complications in interventional procedures, cardiac surgery and percutaneous interventions are also discussed. The great importance of long-term monitoring of patients is emphasized. Infectious vasculopathies are discussed as causes of strokes due to inflammatory changes and vascular lesions. The location, pathogenesis, symptoms, and treatment of brain lesions in viral infections are presented. The contribution of the monograph is the presentation of up-to-date information on thrombotic or thromboembolic cerebral infarctions in patients with COVID-19.

The causes of the occurrence and the methods for diagnosis and treatment of cerebral infarctions in dissections of the extracranial arteries and aorta are described. Despite the low incidence of strokes in Fabry disease and migraine, their diagnosis is important because they are risk factors in young people. A typical constellation of a cryptogenic ischemic cerebral infarction in carcinoma has been presented.

The typical constellation of cryptogenic ischemic strokes in cancer is presented.

Hypercoagulability states are also discussed in detail as a cause of stroke. Various autoimmune and rheumatic diseases have been extensively examined, including systemic lupus erythematosus, moya-moya, Behcet's disease, Takayasu's disease, Kawasaki's disease, giant cell nodular polyangiitis, and others. Rare syndromes (Susac, Cogan, etc.) are presented, which should also be discussed in cryptogenic stroke. In the subsection "Genetic factors" the author publishes her own observations in three patients with ACDs, which occurred in thrombosis of dural sinuses or disorders of arterial circulation. What they have in common is their young age and the presence of a 677 C / T mutation for MTHFR, which is associated with a high risk of ischemic stroke.

The monograph summarizes many etiological and pathogenesis factors for the occurrence of strokes in different age groups. Some of them are really very rare but knowing them will certainly improve the diagnosis and reduce the number of cryptogenic strokes.

*Undoubtedly, the monograph will be useful for a wide range of specialists and students in the field of neurology, cardiology, rheumatology, genetics, and others. Due to all this, the monograph /M/ has great scientific-theoretical and scientific-practical significance.*

In several review and original publications / II, III 7, 11, 20, 22, 25, 28, 34; IV 4.1.6, 4.1.7, 4.1.8, 4.1.9, 4.1.10, 4.1.11, 4.1.12, 4.1.14, 4.1.20, 4.1.21, 4.2.3, 4.2.6, 4.2.12, 4.2.14 / Dr. Dimitrova DM makes an analysis of the Risk Factors for the emergence of CVD. For the timely diagnosis of atrial fibrillation, such as RF for stroke, she suggests long-term telemonitoring in patients /M; IV 4.2.12/. In a modern aspect, along with non-drugs instruments, she discusses the place of antiplatelet agents and new anticoagulants in primary and secondary prevention of stroke. For the timely conduct of differentiated medical, endovascular, or surgical treatment, the strict organization of emergency research in stroke is important /incl. CT and angiography/. The own experience of endovascular treatment in bilateral dissection of the carotid arteries is reflected /IV 4.2.3/. The poster "Revascularization results in interventional treatment of ischemic stroke - clinical cases" /IV 4.1.8/ was awarded the first prize at the V<sup>th</sup> National Congress with international participation of the Bulgarian Association of Neurosonology and Cerebral Hemodynamics /2019/. Data (III 20) has been reported for the triggering of a proinflammatory response in the stroke area due to aseptic inflammation and a predisposing effect of systemic immune suppression to the occurrence of a secondary bacterial infection. Rare clinical cases with cerebral venous thrombosis, cerebral hemorrhage with left ventricular assist device and spontaneous subdural hematoma after exercise are interesting / IV 4.1.10, 4.1.14, 4.1.5 /. **The description of spontaneous cerebral hemorrhage in rivaroxaban-associated thrombocytopenia / IV 4.2.14 / is one of the few in the world literature.** *The scientific production of Dr. Dimitrova, MD in the field of ACD has scientific and practical significance.*

**Spinal pathology.** A significant part of the scientific works is dedicated to spondylodiscitis /III 2, 3, 32, IV 4.1.2, 4.1.3, 4.2.2/. The cases of spondylodiscitis with a rare cause in an immunocompromised patient and the rare SAPHO syndrome (IV 4.1.2, 4.1.3) stand out. Of interest are several scientific reports of clinical cases with peripheral neurological symptoms: spinal epidural lipomatosis, in which causes other than chronic alcohol abuse have been ruled out; acute inferior paraplegia with dysmetabolic changes; hyperkalemic paralysis, / IV 4.2.13, III 29 /. *These studies have scientific and practical significance.*

**COVID-19.** In her monograph / M / Dr. Dimitrova, DM also draws attention to the infection with COVID-19. She enriches our literature with articles and scientific messages presented at international forums, which reflect *her own experience* with neurological complications in COVID-19 and SARS-Cov-2 /III 30, III 33, III 26; IV 4.2.19, 4.2.20/. *These studies have theoretical and practical contribution.*

**Others.** The publications and scientific reports included in this section reflect the broad interests of Dr. Dimitrova, MD. She published up-to-date data on the early diagnosis, including with biomarkers of Alzheimer's disease, shared her personal results from treatment with memantine hydrochloride /III 12, 16, 19/. Pays attention to the frequent craniocerebral injuries and the associated post-traumatic headache /III 1, 4/. Publishes data on the problems of diabetic polyneuropathy and the treatment of neuropathic pain /II 15, 17, 13/. Of interest are the clinical observations in probable Creutzfeldt-Jacob disease, Heidenhain variant /IV 4.2.15/; of cryptogenic meningitis in an immunocompromised patient with systemic rheumatic disease /IV 4.2.17/ and of comorbidity of acute demyelinating polyradiculoneuropathy type Guillain-Barré with neuroborreliosis / IV 4.2.16 /.

**Scientific activity.** Dr. Dimitrova, MD has participated in several international and national congresses. She has been a sub investigator in several clinical trials in the field of MS and stroke.

**Teaching activities.** Dr. Dimitrova MD conducts training in emergency medicine for medical students from MU, Sofia. For the period 2018 - 2020 she has 155 hours of lectures and exercises; there are 1866 hours of extracurricular activities; there are 500 hours of teaching and methodological activity. Its total workload is 2521 hours. She trains 7 residents in neurology.

**Personal qualities and skills.** Dr. Dimitrova, MD speaks English. She has excellent computer literacy.

**Memberships.** Dr. Dimitrova, MD is a member of the Bulgarian Medical Union, Bulgarian Society of Neurology, Bulgarian Society of Neurosonology and Cerebral Hemodynamics, Bulgarian Society of Somnology, European Society of Neurosonology and Cerebral Hemodynamics.

**Teamwork.** The successful work of Dr. Dimitrova deserves a positive assessment, not only with neurologists, but also with scientists from other specialties - electrophysiology, genetics, immunology, imaging, and others.

**Cited and impact factor.** According to the official report, the works have been cited **18** times in Bulgaria. The total impact factor of the actual publications is **56.78**.

### **Conclusion**

Based on the importance of the materials presented by the candidate in the competition, their significant scientific, scientific-applied and scientific-practical contributions, combined with her clinical and teaching activities, I believe that Dr. Maria Dimitrova, MD even exceeds the requirements and criteria of The National Regulations for the conditions and the order of acquiring scientific degrees and holding a position of academic activities in the University Hospital "N. I. Pirogov, Sofia.

All this gives me reason to give my positive opinion and to recommend to the esteemed members of the Scientific Jury to support the candidacy of Dr. Maria Ivanova Dimitrova, MD for the academic position of "Associate Professor" in Neurology at the University Hospital "N. I. Pirogov", Sofia.

07.06.2021

Sofia

**Prof. Dr. Stefka Yancheva, MD**