

Review

By Prof. Margarita Dimova Gospodinova, MD, PhD

**Department of “Infectious diseases, Parasitology and Dermatovenerology”
Medical University – Varna**

Chief of the Scientific Jury determined by order

№ R - 109-87/21.03.2024 from the Rector of the MU-Varna

Regarding: a competition for acquiring of the Academic position “Associate Professor” of scientific specialty “Infectious Diseases”, for the needs of the Department of “Infectious Diseases, Parasitology and Dermatovenerology”, MU-Varna and First Clinic of Infectious Diseases, University Hospital “St. Marina” – Varna, announced in SG 07/23.01.24, with a single candidate Iliyan Todorov Todorov, MD, PhD, who is a Chief Assistant in the Department of “Infectious Diseases, Parasitology and Dermatovenerology” and First Clinic of Infectious Diseases, University Hospital “St. Marina” – Varna.

Documents for the participation in the competition are in compliance with the requirements of the Law on The Development of Academic Staff in Republic of Bulgaria, the Regulations for its application and the Regulations for the Development of the Academic Staff of Medical University – Varna about occupying the Academic Position “Associate Professor”.

I . Analysis of the candidate's professional development.

Ch. Assist. Iliyan Todorov Todorov, MD, PhD graduated from the High School of Mathematics and Natural Sciences "Academician Ivan Ghiuselev", Gabrovo, specialty "biology". In 2012 he graduated with excellent grades at MU – Varna, acquiring a Master's degree in Medicine. After successfully passing an assistant competition in 2013, he started working as an assistant at the Department of “Infectious Diseases, Parasitology and Dermatovenerology”, MU-Varna and as a physician at the First Clinic of Infectious Diseases, University Hospital "St. Marina", Varna. In 2017, he acquired a specialty in infectious diseases (№3835, registration №021003/07.06.2017). In the same year, he was enrolled as a PhD student in an independent form of education at the Department of “Infectious Diseases, Parasitology and Dermatovenereology”,

MU-Varna (Rector's Order №-109-364, from 23.10.2017). In 2020, he acquires educational and scientific degree "PhD" in the specialty of "Infectious Diseases", (Diploma №388/22.05.20). The topic of his dissertation is "Changes in the serum amyloid A protein in the course of some infectious diseases with viral etiology". From 2021 until now, I. Todorov, MD, PhD is a "Ch. Assist" at the Department of "Infectious Diseases, Parasitology and Dermatovenerology", Medical University "Prof. Dr. Paraskev Stoyanov", Varna. Ch. Assist Iliyan Todorov, MD, PhD participates in the education of students in medicine, dental medicine, trainee doctors and other specialists in the medical care, in Bulgarian and English study programs. Actively participates in the scientific activities of the Department. He is fluent in written and spoken English and Russian. He is a member of the Scientific Society of Infectious Diseases in Bulgaria, Bulgarian Medical Association, Union of Scientists in Bulgaria. He has a very good computer literacy.

II. Scientific activity

In the present competition, Ch. Assist. Iliyan Todorov, MD, PhD presents scientific production, covering the minimal scientific and metric requirements of the MU – Varna for occupying of the Academic Position "Associate Professor", specified in the list №1 of the attached documents:

- ✓ Dissertation for acquiring educational and scientific degree "PhD", (A1) – 1;
- ✓ Habilitation – monograph (B3) – 1: Clinical course, severity and prognosis of COVID-19 in patients with comorbidity, First edition, 2022, MU-Varna, ISBN 978-619-221-419-7, with a total volume of 232 pages.
- ✓ Publications and reports, published in scientific journals, referenced and indexed in world-known databases of scientific information, (G7) – 3;
- ✓ Publications and reports, published in non-refereed journals with scientific review or published in edited collective volumes, (G8) – 12;

The scientific data can be summarized and compared with the recommended quantitative requirements for occupying the academic position of "Associate Professor" at MU-Varna and are summarized in the following table:

Table 1. Minimum required points by groups of indicators for Academic Position "Associate Professor"

Group of indicators	Content	"Associate Professor" (number of points)	Ch. Assist. Iliyan Todorov, MD, PhD
A	Indicator 1	50	50
B	Indicator 2	-	-
C	Indicator 3	100	100
D	A total of the indicators from 5 to 9	200	200
G	A total of indicators from 10 to 12	50	50
Total:		400	400

Apart from the minimum scientific indicators, the applicant submits 1 full-text publication in a Bulgarian scientific edition with ISSN (List №2 of the attached documents). There are 4 more full-text publications that are not subject to review in this competition (List №3 of the attached documents) as they were used in a previous procedure for acquiring educational and scientific degree "PhD".

Ch. Assist I. Todorov, MD, PhD is an independent author of a monographic, habilitative work – B3. Of the scientific works carried out in cooperation, he is the first author in 7 of them – G7/1, G8/1, G8/2, G8/6, G8/8, G8/9, G8/11, second author in 6 – G7/3, G8/3, G8/4, G8/7, G8/10, G8/12, and in 2 – G7/2, G8/5 is third author.

For participation in this competition, the candidate applies evidence (reference №899/07.11.2023, MU-Varna Library) for a total of 6 citations reflecting his scientific activity – 2 in publications referenced and indexed in world-known databases with scientific information and 4 in non-refereed journals with scientific review. Autocitations by all authors are excluded. The author's individual h-index stands at 4 according to Google Scholar. The scientific research activity of Ch. Assist. I. Todorov, MD, PhD is focused on the clinical course, methods of diagnosis and treatment of various infectious diseases. His scientific interests are thematically united in the following areas:

Publications, concerning the clinical course, laboratory diagnostics and prognosis of some infectious diseases of viral etiology – №A1, B3, G8/11:

The dissertation of Ch. Assist. I. Todorov, MD, PhD (A1) examines in detail the importance of serum amyloid A protein (SAA) in the diagnostic and therapeutic process in the infectiously ill patient, presenting evidence-based information about this modern laboratory marker, whose values increase, even in the course of viral infections. The dynamics in its values allows timely and precise assessment in terms of severity of course, effect of treatment and prognosis of the outcome of the disease. In recent years, its role in choosing optimal etiological therapy has been increasingly studied. Its clinical value for optimizing hospital stay and prevention of nosocomial infections is also analyzed. So far, the indicator in Bulgaria has not been tested among infectious patients. Therefore, based on information from the scientific literature, the author believes that the in-depth knowledge of the changes in its serum concentrations in some infectious diseases of viral etiology is particularly relevant and would contribute to improving the diagnostic process, resolving some differential diagnostic difficulties, as well as early reporting of complications, effect of the applied treatment and outcome of the disease. The idea of including it as part of the mandatory laboratory minimum for patients with infectious diseases is also outlined, which justifies the actuality of the developed study. For the first time in Bulgaria, a clinical study was conducted on the changes that occur in serum concentrations of SAA in patients suffering from acute infectious diseases of viral etiology. For the purpose of the study, a modern analytical method for the study of SAA in a minimum amount of serum was adapted, which can be used in the inclusion of the indicator as part of the laboratory minimum among patients with acute infectious diseases.

The author develops and enriches his interest in viral infections through his habilitation work on "Clinical course, severity and prognosis of COVID-19 in patients with comorbidity". The monograph is structured in several sections, with the first part presenting modern and comprehensive data on the coronavirus family. Their most characteristic feature is the ability to "jump" the animal world and reproduce among the human population, causing previously unknown diseases. The experience and achievements of a number of authors in the fight against inbreeding severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) are highlighted. COVID-19 is considered in a propaedeutic aspect, as the author describes the specific features in the morphology of the causative agent, the mechanisms of infection, pathogenesis, clinical manifestation. Successes in the development of modern methods of express diagnostics are reported. The main points in treatment and prevention, especially in patients belonging to the risk groups for severe course, are also mentioned. The main part of the monograph examines the

COVID-19 relationship and comorbidity. The severe clinical course of the disease and its often fatal outcome in adult patients raises the issue of chronic, concomitant diseases as a major risk factor determining the evolution of the disease. The review part presents in detail the symptoms, possible complications and prognosis of COVID-19 in patients suffering from respiratory, cardiological, gastroenterological, hematological, orthopedic and neurological diseases. The possibility of a two-way influence was discussed. The need for an interdisciplinary approach in these cases is determined. In the part with own observations are presented the results obtained after an investigation of patients with COVID-19, where data on comorbidity are available. Important conclusions for the practice are reported. The number of comorbidities significantly affects the clinical course of COVID-19. The manifestations are more severe the more pronounced the comorbidity, especially if it is in combination with advanced age and a long period of outpatient treatment. The outcome and prognosis of COVID-19 are significantly worse among patients with a higher number of concomitant diseases. About all patients, the Charlson Comorbidity Index (CCI) has been calculated, according to which the long-term prognosis of COVID-19 is largely determined by the nature, nature and number of accompanying chronic, noncommunicable diseases.

In publication №G8/11, the author presents the main characteristics of the infection caused by human metapneumovirus – an emerging infectious agent whose clinical significance is associated with high morbidity and mortality from acute respiratory infections, mainly in childhood and among immunocompromised. The knowledge of medical staff in this direction is decisive for the construction of adequate diagnostic and therapeutic behavior, on which the prognosis of the outcome of the disease depends.

Publicationsp concerning the characteristics in the clinical course of mixed infections – №G7/3, G8/3, G8/4:

A team of authors with the participation of Ch. Assist. I. Todorov, MD, PhD presents a clinical case of mixed infection with *Yersinia enterocolytica* and *Astrovirus* (№G7/3) in a 1-year-old child. The clinical course here is usual, without the development of complications, incl. without evidence of tightened course or formation of a healthy vector in the period of convalescence. Fundamental to the favorable outcome are the timely diagnosis and the initiation of appropriate antibacterial

therapy. A fulcrum in the construction of the differential diagnostic plan are the data from the epidemiological history of consumption of poorly heat-treated food and close contact with animals.

Ch. Assist. I. Todorov, MD, PhD presents two cases of acute hepatitis B with a delta agent /co-infection/ without hepatic coma, occurring against the background of chronic hepatitis C (№G8/3) and four cases of chickenpox and scarlet fever in children hospitalized in the Infectious Clinic (№G8/4), taking into account that the mixed form of acute viral hepatitis (HBV+HDV+HCV) is relatively rare in patients in the Varna region. The reason for polyetiological is rooted in the combination of several risk factors in each particular patient. The high hepatocytolysis (ALAT > 1000IU/l) and the severe clinical course of the disease allow the simultaneous infection of the individual with HBV and HDV as the most likely. The combination of several etiological agents in the same patient increases the likelihood of clinical and biochemical relapse in the course of the evolution, with one-time relapses having a good prognosis.

The incidence of mixed infection chickenpox and scarlet fever remains relatively low for the Varna region, the age up to 5 years is mainly affected, and the clinical course is a moderate, with no lasting consequences for the patient, both in the short or long term. In all observed patients, initial vomiting was absent, which could be explained by possible functional suppression of erythrogenic exotoxin by varicella virus under conditions of mixed infection. In all patients, the symptoms of chickenpox precede the manifestations of scarlet fever, on the basis of which it could be assumed that it is a secondary infection with beta-hemolytic streptococcus.

Publications concerning the development of complications from various organs and systems in patients with infectious diseases – №G7/1, G8/1, G8/2, G8/6, G8/7, G8/8, G8/9:

A significant part of the scientific works of Ch. Assist. I. Todorov, MD, PHD are devoted to the study of possible complications in the course of certain infectious diseases involving different organs and systems. Emphasis is placed on complications affecting the urinary system. The author makes important conclusions for practice that acute post-streptococcal glomerulonephritis is a disease with a favorable prognosis. Prevention of the cases consists in the timely and adequate treatment of scarlet fever, including 10 days of administration of an antibiotic, in combination with an antihistamine.

Cytomegalovirus (CMV) infection leads to various complications in the infected person's body, predominantly affecting the kidneys, mainly after transplantation or perinatally. Proteinuria is recorded relatively often in children with various infectious diseases. It is usually a transient

phenomenon that is due to general intoxication or is the result of the involvement of the renal parenchyma in the general inflammatory process. The persistence of the symptom after illness requires clarification by a nephrologist.

Kidney damage in the course of diarrheal infections occur frequently. They are especially characteristic of cholera, salmonellosis, colienteritis, dysentery. They are due to developing toxic, hypoxic and dysmetabolic processes leading to nephritis, pyelitis, pyelonephritis, renal failure. Timely and proper treatment correlates with a favorable outcome and prognosis.

Neurological complications develop in a small part of all cases of hospitalized patients with chickenpox in the Clinic of Infectious Diseases- Varna. Most often, cases of acute cerebellitis or "diffuse" encephalitis are recorded. The prognosis is favorable. The determining factor for the final outcome remains the early initiation of specific antiviral treatment. A potential risk point is the intake of corticosteroids in the incubation period of the disease.

Hemolytic-uremic syndrome (HUS) is a form of thrombotic microangiopathy occurring clinically with a triad of symptoms: hemolytic anemia, thrombocytopenia, acute renal impairment. It develops as a complication in the course of enterohemorrhagic colienteritis or infection with Shiga-toxin producing *Shigella dysenteriae*. There are known cases etiologically related to streptococci or various genetic mutations. Treatment involves pathogenetic and symptomatic agents, and antibiotics often worsen the course. The prognosis is serious, often leading to hemodialysis.

Nephrotic syndrome is a rare but possible complication in the course of chickenpox. It manifests itself with a typical clinical presentation, without negatively affecting the underlying disease. The treatment is typical as it is carried out in collaboration with a nephrologist.

Publications concerning various problems in infectious pathology - №G7/2, G8/10, G8/12:

Ch. Assist. I. Todorov, MD, PhD participates in studies about fecal calprotectin and its role as a laboratory marker occupying an important place in the diagnosis of gastrointestinal infectious diseases. It is most widely used in cases of enterocolitis caused by *Clostridium difficile*. Its study allows timely and adequate discrimination of cases with bacterial from those of viral etiology. Its levels correlate with disease severity. The study of fecal calprotectin is economically viable and non-invasive, which allows wide application in clinical practice.

Infections among transplanted individuals are a current problem these days, due to the relatively high frequency with which they are registered. Recipients are a particular risk group for infectious diseases of a different nature, in which the outcome of the illness often turns out to be fatal. That is why conducting specific prophylaxis, making an early diagnosis and undertaking adequate treatment are the main determinants for preserving the lives of patients.

It is evident from the presented evidence that the contributions from the scientific production of Ch. Assist. Iliyan Todorov, MD, PhD concerns contemporary and current topics in the field of infectious diseases, most of which the author studies for the first time in Bulgaria. The practical orientation of the publications significantly supports the activity of the physicians in the direct contact with the patient. The relevance of the presented scientific activity can also be judged from citations in journals, with scientific review, including in such referenced and indexed in world-known databases. The presented reference for the original scientific contributions reflects the scientific activity of the candidate and his lasting interest in various and topical topics in the field of infectious diseases.

III. Teaching activities

Dr. Todorov's teaching activity dates back to 2013. He conducts practical exercises in infectious diseases to medical and dental students, as well as training of trainee doctors in Bulgarian and English language. For the past two years he has been lecturing medical and dental students in English. He also conducts practical exercises in infectious diseases and students as health inspectors at the Medical College. Dr. Todorov's workload exceeds what is required. The workload reference issued by the Medical University – Varna, attached to the general set of documents for participation in this competition, shows that for the period from 2018/2019 to 2022/2023 the report on workload is attached to the general set of documents for participation in this competition. Ch. Assist. Iliyan Todorov, MD, PhD has from 308 to 433 academic hours per academic year, according to a norm (by decision of the AC of MU - Varna) of 220 hours.

IV. Conclusion:

My first impressions of Ch. Assist. Iliyan Todorov, MD, PhD are from his scientific years. Ambitious, hardworking, excellent student. A competent young infectionist, gaining experience and new knowledge over the years, has grown in front of my eyes, showing exceptional activity in

mastering diagnostic methods and therapeutic approaches in infectology. Ch. Assist. Todorov, MD, PhD is a respected lecturer of students and interns, he is a colleague you can rely on in the team.

According to the presented scientific and teaching indicators Ch. Assist. Iliyan Todorov Todorov, MD, PhD fully meets the requirements for occupying the Academic Position of "Associate Professor" in accordance with the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for the Development of the Academic Staff of MU-Varna.

On the basis of the above, I give my positive assessment of the candidate in the competition and recommend to the members of the Scientific Jury to award to Chief Assistant Iliyan Todorov Todorov, MD, PhD the Academic Position "Associate Professor" in the scientific specialty "Infectious Diseases" for the needs of the Department of "Infectious Diseases, Parasitology and Dermatovenerology" at MU-Varna and the First Clinic of Infectious Diseases in the University Hospital "St. Marina" - Varna.

20.05.2024
Varna

Prof. M. Gospodinov
Chief of ES "Infectious diseases"
Department of Infectious Diseases, Parasitology and Dermatology, MU - Varna

Заличено на основание чл. 5,
§1, б. „Б“ от Регламент (ЕС)
2016/679