

REVIEW

By Assoc. Milena Krasimirova Bozhkova, MD, PhD

Department of Microbiology and Virology

MU-Varna

Subject: Dissertation for awarding the educational and scientific degree "**Doctor**"

Dr. Victoria Snezhanova Snegarova – Toneva

With the topic of the dissertation:

"Evaluation of the HB&L Automated System for Rapid Diagnosis of Urinary Tract Infections"

Professional field 4.3 Biological Sciences

Doctoral Program in Microbiology

Supervisor: Prof. Temenuga Stoeva, MD, PhD

General presentation of the PhD procedure:

Dr. Viktoria Snezhanova Snegarova – Toneva has presented a set of materials on electronic and paper form, which are in accordance with Article 69 of the Regulations for the Development of the Academic Staff of MU-Varna. The set includes a project for an abstract, dissertation, publications and scientific participations – original and lists. 4 (four) full-text publications and 3 (three) scientific participations (two posters and one oral presentation) were attached in connection with the dissertation.

Brief biographical data:

Dr. Victoria Snezhanova Snegarova – Toneva was born on 10.01.1983. in Varna, where she completed his secondary education, and subsequently higher, with a master's degree in medicine at the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. Since 2013, she has a recognized specialty in microbiology, and subsequently in virology - since 2022. In year 2013. she also obtained a master's degree in Health Management at the same university. Dr. Snegarova is a long-time assistant professor at the Department of Microbiology and Virology at MU-Varna and at the same time works as a microbiologist and virologist at Medical Diagnostic Laboratory "Laborexpress 2000", where she is currently practicing. She is fluent in English and French.

Description, relevance and significance of the topic:

Dr. Snegarova's dissertation is an interesting and in-depth scientific work that focuses on the importance of a repeatedly analyzed, but still unresolved general medical problem – the accurate and fast diagnosis of urinary tract infections. The introduction of automated systems for rapid diagnosis of urinary tract infections in clinical practice has the potential to significantly support and even replace classical methods, mainly due to the significantly shorter time interval required for the analysis. In this sense, there is a clear need for precise studies to analyze their accuracy.

Given the high incidence of these diseases in all age groups, both outpatient and inpatient, the potential risks for the patient in case of improper and/or untimely treatment, I define the importance of the topic as indisputable.

The dissertation presented to me contains 134 pages, with references to 285 literary sources and consists of the following parts: introduction, literary review, purpose and objectives, materials and methods, results and discussion, conclusions, contributions of the dissertation, publications related to the dissertation, literature used.

In the **introduction**, Dr. Snegarova makes a brief overview of the significance of the problem, setting out the main criteria for defining urinary tract infections and the "gold standard" in their diagnosis – standard uroculture, and emphasizing the importance of implementing significantly faster automated microbiological screening systems in clinical practice.

The Literature Review Urinary tract infections is an in-depth analysis of many of the significant aspects of urinary tract infections and contains useful and up-to-date information on the classification, epidemiology, etiological spectrum and risk factors for urinary tract infections. The dissertation has paid special attention to the methods for diagnosing urinary tract infections, including sufficient information in terms of volume and content both for classical ones and for alternative modern methods, including those based on molecular genetic tests and proteomic analysis. Of particular interest in the review is the in-depth analysis of the methods for proving residual antimicrobial activity in urine. Its determination is an important aspect of the overall diagnostic process, as it is a common cause of discordance between clinical symptomatology and microbiological finding. In the review part, many correctly selected literature sources are used, mainly from the last 5 years.

Dr. Snegarova sets out a clearly formulated **goal** of her dissertation, namely: to evaluate the automated HB&L Uroquattro system for performing rapid diagnosis of urinary tract infections. To achieve it, a total of six **tasks have been set**, which fully correspond to the goal and are its logical continuation.

At the beginning of the section "**Materials and methods**", the design of the study, the inclusion and exclusion criteria are clearly described. All microbiological methods used (conventional and automated) are described in detail and correctly, which allows them to be used by other researchers in the same field. The methods for statistical data processing are skillfully selected and presented accurately and clearly. The prospective nature of the study and the large number of urine samples examined (n=1600) of outpatients is a necessary condition for its representativeness.

The presentation in the section "**Results and discussion**" follows the tasks set and is presented on 46 pages. The analysis of the etiological spectrum of UTI legitimately shows the dominance of Gram negative bacterial flora with a distinct predominance of *E. coli* in both sexes. The data are presented graphically and in tables, and I would recommend combining the data from Tables 2 and 3 into one. Dr. Snegarova has paid special attention to specific groups of patients – after kidney transplantation, patients with a urinary catheter, with a nephrostomy and pregnant women. The comparative assessment of the HB&L Uroquatro automated system with the classical culture-based method – uroculture occupies an important place in the structure of Dr. Snegarova's dissertation. The data obtained by her for only nine discrepancies (defined as negative by HB&L Uroquatro, positive in culture testing) in 1600 clinical samples examined determined a positive predictive value for the rapid automatic screening of 100%, a negative predictive value - 99.3% and an overall accuracy of the method of 99.4%. The data obtained are skillfully compared with data from other authors and the possible causes of such discrepancies are analyzed in detail. The results of the determination of antimicrobial susceptibility of all isolates were analyzed, and the resistance profiles of the HB&L Uroquatro automated system were compared with those determined by the Kirby-Bauer disc-diffusion method and the Vitek2 automated system. In general, Dr. Snegarova found a very good correlation (ranging between 90.5 and 100%, an average of 94.8%) in the 60 isolates examined. Minor, major and very major errors (mE, ME and VME) are detected and analysed, the potential causes for them and the possible consequences in determining the therapeutic regimens of patients. Of particular interest is the determination of the indicator "Residual antibiotic activity" (RAA) through the HB&L system in the examined urine samples. This indicator is an important benchmark for the clinical microbiologist and its determination would significantly support the overall diagnostic process. Residual antibiotic activity is found in a relatively high percentage of the examined urine samples (5.7%), which is an important evidence of pre-test use of antibiotics or phytopreparations.

Based on the results of her study, Dr. Snegarova formulated 10 main conclusions. All **conclusions** are logically derived from the data obtained and are correctly formulated.

The dissertation contains several **scientific and applied scientific achievements**. New means are used to prove significant new aspects of existing scientific problems. The main

contributions of the dissertation are divided into the following directions: original, confirmatory and scientifically applied. I accept all of them, considering it particularly important to determine a laboratory algorithm, including screening of the urine sample, followed by a microscopic examination and a rapid study of antibiotic sensitivity directly from a clinical sample.

In conclusion, I believe that the dissertation of Dr. Victoria Snegarova-Toneva is a complex and in-depth study on an interesting and topical problem of modern clinical microbiology. It is a well-conceived and precise methodologically grounded study, it is carried out very accurately and is presented excellently. The data obtained are clearly and conscientiously discussed and contribute to expanding the available knowledge about the microbiological aspects of UTI. The results of the study make an original and theoretically applied contribution to clarifying the role of the HB&L automated system for the rapid diagnosis of urinary tract infections, and the potential widespread application of this system for the development of optimized new diagnostic and therapeutic strategies.

The presented work meets the legal requirements for acquiring the degree of "Doctor" in the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its application and the criteria for awarding scientific degrees laid down in the Regulations for the Development of the Academic Staff at MU-Varna. Based on all of the above, as a reviewer, I confidently express my positive opinion on the dissertation and in my capacity as a member of the Scientific Jury, I give **my positive vote** for awarding the educational and scientific degree "Doctor" in the field of higher education 4. "Natural Sciences, Mathematics and Informatics", professional field 4.3. Biological Sciences, in the scientific specialty "Microbiology" of Victoria Snezhanova Snegarova - Toneva.

Varna

20.01.2025

Reviewer:

/Assoc. Dr. Milena Bozhkova, MD/

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