

REVIEW

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Chairman of the Scientific jury, appointed by order No. R-109-436/17.10.2025
of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov" Varna, Bulgaria

Regarding: the award of the educational and scientific degree "Doctor of Philosophy" (PhD) in the doctoral program "Surgery", within the area of higher education "7. Healthcare and Sports", professional field "7.1. Medicine"

Dissertation on the topic: "Microbiological profile of purulent-septic diseases in maxillofacial surgery"

Author: Iliana Dimitrova Mechkarova, MD, DMD – a full-time doctoral candidate in the procedure for the award of the educational and scientific degree "Doctor of Philosophy" at the Department of General and Operative Surgery, Faculty of Medicine at the Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria.

Doctoral program: "Surgery"

Scientific supervisor: Assoc. Prof. Yanko Georgiev Yankov, MD, PhD

1. General presentation

This review has been prepared on the basis of order No. R-109-436/17.10.2025 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria, by which I have been appointed as Chairman of the Scientific jury for the current procedure.

The submitted set of materials, in hard copy and electronic format, is in full compliance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB) and Art. 44 (3) of the Regulations for the Development of the Academic Staff at the Medical University of Varna, Bulgaria.

The doctoral candidate, Iliana Dimitrova Mechkarova, has enclosed 2 scientific publications on the topic of the dissertation, which meet the minimum national requirements according to the respective group of quantitative and qualitative indicators for the award of the educational and scientific degree "Doctor of Philosophy".

The dissertation submitted for review is current, logically structured, and contains all the mandatory parts of a dissertation thesis – introduction, literature review, aim, objectives, materials, methods, results, discussion, conclusions, contributions, and bibliography.

2. Biographical information about the doctoral candidate

Dr. Iliana Dimitrova Mechkarova holds a Master's degree in Dental Medicine from the Medical University of Plovdiv, Bulgaria, after which she also obtained a Master's degree in Medicine from the Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria. Her professional development is associated with the Clinic of Maxillofacial Surgery at University Hospital "Sveta Marina", Varna, Bulgaria, where she completed her residency and obtained a specialty in oral surgery. Since 2022, she has been enrolled as a full-time doctoral candidate at the Department of General and Operative Surgery at the same university hospital. Dr. Mechkarova has actively participated in a number of scientific forums, which is indicative of her sustained interest in scientific research and her professional growth.

3. Relevance of the developed topic

The topic chosen by Dr. Mechkarova is extremely current and holds immense clinical and practical significance. In the context of the global crisis related to antimicrobial resistance (AMR), the empirical therapy for severe bacterial infections is becoming one of the greatest challenges facing modern medicine. Purulent-septic diseases in the maxillofacial region (MFR), which often manifest as deep and life-threatening phlegmons, require immediate and adequate antibiotic intervention, alongside surgical treatment.

The relevance of the work is reinforced by the fact that international guidelines, although useful, cannot reflect the unique local characteristics of the microbial landscape. The present study addresses precisely this gap, representing the first large-scale analysis of its kind of the microbiological profile in one of the country's largest hospital centers over the last ten years. This provides a scientific basis for a critical revision and optimization of existing therapeutic protocols, which will directly contribute to reducing therapeutic failures and the risk of severe complications such as sepsis and mediastinitis.

4. Structure and volume of the dissertation

The dissertation is structured in accordance with all academic requirements and represents a complete and in-depth scientific study. The total volume is 133 pages, with the content being illustrated by 13 original graphics and 13 detailed tables that present the results in a clear and accessible manner. The bibliography is comprehensive, including 140 literary sources, 136 of which are in the Latin script, which demonstrates the doctoral candidate's excellent awareness of current global trends regarding the issue. The structure of the work is logical and coherent,

encompassing all the mandatory components – introduction, literature review, aim, objectives, materials, methods, results, discussion, conclusions, and contributions. The Author's Summary has been prepared correctly and fully reflects the content and contributions of the dissertation.

5. Aim and objectives of the study

The main aim of the dissertation is precisely formulated: to conduct an in-depth retrospective analysis of the microbiological profile of purulent-septic diseases in the MFR, treated at University Hospital "Sveta Marina", Varna, Bulgaria over a 10-year period, and to create a current "microbiological map" for the region.

To achieve this aim, the doctoral candidate has defined four specific and logically connected **objectives**:

1. Determination of the overall etiological structure of the infections.
2. Comparative analysis of the microbiological profile in cases of odontogenic and non-odontogenic origin.
3. Tracking the dynamics of the main causative agents over time by comparing two five-year periods.
4. Analysis of the frequency of polymicrobial infections and of samples without a proven causative agent.

I consider that the stated aim and objectives are adequate, operationally defined, and fully correspond to the scope of a dissertation study for the award of the educational and scientific degree "Doctor of Philosophy".

6. Materials and methods

The study is based on a retrospective analysis of vast clinical material – 1735 samples from patients with purulent-septic diseases in the MFR, treated at the Clinic of Maxillofacial Surgery at University Hospital "Sveta Marina", Varna, Bulgaria, over a 10-year period (2015-2024). This scale ensures exceptionally high statistical power and reliability of the obtained results. The methodology is correctly described and is fully appropriate for the stated aim. The clinical material is stratified according to the origin of the infection (odontogenic/non-odontogenic) and is analyzed using adequate methods of descriptive statistics. The study is methodologically sound and provides a reliable basis for drawing valid clinical and microbiological conclusions.

7. Results and discussion

The dissertation work has been developed at a high scientific level, demonstrating both in-depth theoretical knowledge of the problem and excellent practical skills of the doctoral

candidate in planning, conducting, and analyzing a large-scale scientific study. The core of the dissertation consists of the results and their discussion, which are presented at an exceptionally high level.

The doctoral candidate presents a rich and excellently structured body of empirical material. The results are presented systematically and are subjected to an in-depth analysis in the "Discussion" section. The following findings stand out with particular weight and originality:

1. One of the key conclusions, which the doctoral candidate rightly brings to the forefront, is the immense diagnostic challenge posed by the high proportion of samples with "resident microflora" (37.1%). The analysis shows that a large percentage of samples are sterile (28.6%). In her discussion, Dr. Mechkarova thoroughly analyzes the probable causes – prior antibiotic therapy and methodological difficulties in cultivating demanding anaerobes. This finding unequivocally proves why empirical therapy must be based precisely on local epidemiological data, such as those provided by the present work.

2. The most significant and original scientific contribution of the study is the definitive establishment of coagulase-negative staphylococci (CoNS) as the leading group of pathogenic agents (23.0%), surpassing even the classic oral streptococci. This represents a significant paradigm shift in the etiology of these infections. In her discussion, Dr. Iliana Mechkarova skillfully analyzes this phenomenon, which she correctly defines as a "staphylococcal shift," explaining it with a complex of factors, among which the selective pressure from widespread antibiotic use and the potential nosocomial origin of some infections play a leading role. The in-depth analysis of the species composition within CoNS (*S. epidermidis* and *S. haemolyticus*), which are known for their ability to form biofilms and their high methicillin resistance (MRSE), further emphasizes this conclusion and has direct therapeutic implications.

3. The study's results offer an excellent analysis of the pathogenetic mechanisms of key pathogens. A clear distinction is made between the biofilm-mediated, more indolent course with CoNS, and the aggressive, toxin-mediated, and highly abscess-forming potential of *Staphylococcus aureus*. The presence of Gram-negative bacteria (Enterobacteriaceae) is convincingly presented as an "alarming signal" for more severe systemic involvement due to endotoxin (LPS) and their high potential for multidrug resistance (ESBL-producers).

4. The scientific work unequivocally confirms the different microbiological profile in the two types of infections – dominance of streptococci in odontogenic cases and dominance of staphylococci (*S. aureus* and CoNS) in non-odontogenic ones. This conclusion has direct practical value.

5. The classic etiological differentiation for local conditions is confirmed and quantitatively validated – dominance of streptococci in odontogenic and staphylococci (*S. aureus* and CoNS) in non-odontogenic infections. This conclusion alone has immense practical value for the initial orientation of the clinician. In the discussion, however, the doctoral candidate goes further, complicating this model with the analysis of the third most frequent group – Gram-

negative bacteria from the family Enterobacteriaceae. She convincingly proves that their presence is a marker for more severe, complicated, or secondarily infected processes and is associated with a high risk of multidrug-resistant strains (ESBL-producers).

The discussion is at a very high scientific level. Dr. Iliana Mechkarova skillfully compares her results with leading international studies, providing a well-argued explanation for the observed phenomena with factors such as antibiotic pressure, the nosocomial environment, and the influence of the COVID-19 pandemic. The clinical recommendations made are a logical consequence of the analysis and are scientifically substantiated.

The doctoral candidate presents an exceptionally rich empirical material, which is subjected to an in-depth, multifaceted, and critical analysis in the "Discussion" section. It is in this part that Dr. Iliana Mechkarova's scientific maturity and her ability not just to describe but to interpret the data, deriving important clinical implications from them, are most clearly evident.

8. Conclusions and scientific contributions

The seven formulated **conclusions** are clear, concise, and directly follow from the obtained results and the analysis conducted. They summarize the key findings of the dissertation and are as follows:

1. Diagnostic challenge and the role of resident microflora. The analysis of microbiological findings reveals a complex picture, with resident microflora, consisting of more than one bacterial species, being the most frequently observed (50.50% of all samples with growth). This highlights the challenges in etiological diagnostics, as it is difficult to determine a dominant pathogen in such cases. The next most frequent findings are monoinfections with specific pathogens, among which coagulase-negative staphylococci (11.40%), the *Streptococcus viridans* group (10.00%), and Enterobacteriaceae (7.90%) have the highest share. These results necessitate the need for local epidemiological data for adequate empirical antibiotic therapy, especially in polymicrobial infections and in patients who have previously received antibiotics.
2. Leading etiological agents and the significance of Coagulase-negative Staphylococci. Among the pathogenic agents, the leading ones are coagulase-negative staphylococci (23.0%) and streptococci of the *viridans* group (20.1%). The high proportion of coagulase-negative staphylococci establishes them as significant opportunistic pathogens, and not merely contaminants.
3. Clear etiological differentiation according to the origin of the infection. A clear difference exists in the etiology of the infections: in odontogenic infections, streptococci (especially of the *viridans* group) dominate, whereas in non-odontogenic infections, the leading agents are staphylococci (*S. aureus* and CoNS). This conclusion is of essential importance for the choice of initial antibiotic therapy.

4. Anatomical correlations and the origin of odontogenic infections. Over 70% of odontogenic infections originate from the mandible. This correlation is consistent with the anatomical predispositions for the spread of infection in this area, related to greater bone density and the anatomical position of the teeth.
5. Trend of a "staphylococcal shift." Over the last five years, an alarming trend of an increase in isolated staphylococci has been observed, accompanied by a decrease in streptococci. This phenomenon supports the "staphylococcal shift" observed in international literature.
6. Methodological limitations and the role of anaerobes. The low proportion of isolated strict anaerobic bacteria (2.4%) is most likely due to a methodological artifact related to sample collection and transport. This necessitates mandatory anti-anaerobic coverage in the empirical therapy of abscesses and phlegmons, despite the low isolation rates.
7. Significant role of fungi as co-pathogens. *Candida spp.* represent a significant proportion of the isolates (7.9%), which establishes them as an important co-pathogen, especially in odontogenic infections. Their presence requires increased attention to the risk of fungal superinfections, particularly in patients with a compromised immune status or after prolonged antibiotic therapy.

The **contributions** of the dissertation are significant and have both an original and a confirmatory nature, with clear scientific and applied value. The original contributions are:

1. For the first time in Bulgaria, such a large-scale (10-year, over 1700 samples) analysis of the etiology of purulent infections in the MFR has been conducted, which creates an invaluable local epidemiological database.
2. For the first time for the conditions in the country, the phenomenon of the "staphylococcal shift" has been documented and analyzed, which is an original scientific contribution with immense consequences for clinical practice.
3. A current "microbiological map" for the region has been created, which serves as an objective tool for optimizing therapeutic protocols.

The scientific-applied and confirmatory contributions are as follows:

1. The classic etiological differentiation (odontogenic vs. non-odontogenic origin) has been confirmed, which strengthens the pathogenetic understanding in a local context.
2. Scientifically substantiated recommendations for rethinking empirical antibiotic therapy have been developed, which are directly applicable in clinical practice.
3. Demographic analysis has outlined the age group between 31 and 50 years as the most affected, with a clear predominance of the male gender.

9. Analysis of the applied scientific publications on the topic of the dissertation

In support of her work, Dr. Iliana Mechkarova has included **two scientific publications** on the topic of the dissertation, which are not merely a formal fulfillment of requirements but represent an essential element of her research strategy. These articles demonstrate scientific maturity and the ability to validate results at different levels of analysis, lending additional depth and completeness to the dissertation.

1. The first publication, titled "**Etiological spectrum of odontogenic and non-odontogenic abscesses in oral and maxillofacial surgery**" and published in the journal "Scripta Scientifica Medicinae Dentalis" in 2023, can be seen as a concentrated microcosm of the larger dissertation research. Over a one-year period and a sample of 167 patients, Dr. Mechkarova tested and validated her research hypothesis and methodology. The results from this article – the establishment of a high percentage of sterile cultures and the dominance of polymicrobial resident flora – fully correspond to and precede the main conclusions in the dissertation. This publication has important methodological value, as it confirms the relevance of the research problem and the adequacy of the chosen approach even before its scaling up to the massive ten-year dataset.

2. The second publication, "**Microbiological spectrum, clinic and treatment of patients with phlegmons of the mouth floor**" published in the International Journal of Medical Science and Clinical Invention also in 2023, represents a qualitative leap in analysis, moving from general epidemiology to specific clinical prognostics. Focusing on phlegmons – the most severe and life-threatening form of purulent infections – the doctoral candidate provides an exceptionally valuable and original analysis of three clinical cases. Here, Dr. Iliana Mechkarova demonstrates her ability to connect the isolated microorganism with the patient's clinical phenotype. She convincingly shows how the etiological agent correlates with treatment outcome: *Candida albicans* is associated with the oldest patient, with the most comorbidities, and the longest hospital stay; *Streptococcus anginosus* – with the youngest patient and the most severe inflammatory reaction (highest CRP and leukocyte values); and *Staphylococcus epidermidis* – with a milder course and a short stay in the clinic. This analysis is of enormous practical value, as it shows how microbiological findings can serve as a prognostic marker, and demonstrates the author's ability to think as a clinician-researcher, connecting the laboratory to the bedside.

Taken together, these two publications outline a coherent research program – from the validation of methodology in a pilot study to an in-depth clinical analysis of the most severe cases. They transform the dissertation from a static epidemiological report into a dynamic clinical tool with real applied value.

10. Critical remarks and recommendations

The dissertation work is of a high scientific level. As a constructive recommendation with a debatable character, I would point out that future studies in this direction could be enriched by applying molecular-genetic methods (e.g., PCR) for a more precise identification of the fastidious

anaerobic bacteria, whose role, as the doctoral candidate herself notes, is underestimated due to methodological limitations. This remark, however, in no way diminishes the value of the present study.

11. Conclusion

The dissertation of Dr. Iliana Dimitrova Mechkarova on the topic "Microbiological profile of purulent-septic diseases in maxillofacial surgery" is a complete, original, and scientifically substantiated study that fully meets the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Regulations for the Development of the Academic Staff at the Medical University of Varna, Bulgaria for the award of the educational and scientific degree "Doctor of Philosophy".

The author has demonstrated profound theoretical knowledge and excellent skills for independently conducting a large-scale clinical study. The obtained results have high scientific and applied value, and have the potential to change existing therapeutic practices.

Based on the foregoing, I give my **positive assessment** of the dissertation and confidently propose to the esteemed Scientific Jury to award **Dr. Iliana Dimitrova Mechkarova** the educational and scientific degree "**Doctor of Philosophy**" (PhD) in the **scientific specialty of "Surgery"**.

11.11.2025
Varna, Bulgaria

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