

## REVIEW

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*Subject:* dissertation for the acquisition of the educational and scientific degree "PhD" in the Field of higher education: 7. Health and Sport; Professional field: 7.1 Medicine.

**Author:** Dr. Zhenya Stoyanova Borisova, MD

**PhD program:** "Dermatology and Venereology"

**PhD Thesis:** "Clinical, diagnostic and therapeutic studies on common bacterial skin infections in childhood"

**Scientific supervisor:** Prof. Dr. Ilko Bakardjiev, MD, PhD

**Scientific unit:** Department of Infectious Diseases, Parasitology and Dermatovenerology at the Medical University of Varna

I have been appointed as a member of the Scientific Jury (Order No. P-109-213/28.03.2023 of the Rector of MU-Varna) and assigned to prepare a review at the first meeting of the Jury.

The submitted set of materials on paper and electronic media complies with the requirements of the regulations in the country and in MU-Varna.

### **1. Relevance of the dissertation topic:**

Bacterial infections of the skin (pyodermias, purulent dermatitis) have the highest frequency among dermatological diseases, and those in childhood constitute a significant part of the outpatient practice of the dermatologist. Predisposing conditions for infection are compromised skin integrity, climatic factors (high temperatures, high humidity), concomitant skin diseases (scabies, atopic dermatitis, eczema, pruritus) or metabolic diseases (diabetes, obesity, metabolic syndrome). It should also be borne in mind that more than half of the cases are mixed infections, even with more than two causative agents. Diagnosed in time and treated correctly, skin infections are almost always curable. The lack of data on the demographic

characteristics, social and risk factors in the Varna region, mode of infection, etiology and clinical features in the course of pyoderma in childhood motivated the dissertation to carry out the present studies, and to answer some essential questions useful for clinical practice. In this sense, the dissertation project is relevant and suggests a contributory nature in the development of this socially significant problem.

## **2. Structure, characteristics and evaluation of the dissertation:**

The submitted scientific work is properly structured and contains 141 printed pages, of which 32 pages - literature review, aim and objectives of the study - 1 page, material and methods - 11 pages, results of own studies - 41 pages, discussion of results - 12 pages, conclusion - 3 pages, conclusions and contributions - 2 pages. It is illustrated with 35 tables and 39 figures. It contains a 26-page bibliography with 339 titles - 12 in Cyrillic and 327 in Latin, the Bulgarian experience on the problem is also reflected, reference to publications and participation in scientific forums related to the dissertation - 1 page.

**The literature review** is an analysis of the cited literature sources, and the problem of "pyodermias in childhood" is discussed in a contemporary aspect. The periods of childhood development are indicated, the resident bacterial flora in different topographic regions of the body is described, the epidemiology and etiology of common staphylo- and streptodermias are discussed, and due attention is paid to mixed infections. In her work, the dissertator has discussed a modern nosological classification of pyodermas, indicating both common and rare skin infections in childhood. Due attention has been paid to the rare, but life-threatening, Staphylococcal Scalded Skin Syndrome, Fasciitis necrotisans, Toxic Shock Syndrome. The problem of bacterial resistance is discussed, as well as possible allergic reactions from the use of laqujalne is systemic antibiotics.

**The aim of the dissertation** is clearly stated and focuses on the analysis of the dynamics, demographic and risk factors, clinical, diagnostic and therapeutic aspects of common bacterial skin infections in childhood in northeastern Bulgaria for the period 2012-2018.

The dissertation has set **6 tasks**, the sequential implementation of which logically leads to the achievement of the goal.

**The study material** is a clinical contingent of 303 children - 154 with bacterial skin infection and 149 with other dermatoses, used as a control. All patients met the inclusion criteria for the study, were stratified according to age, those with purulent dermatitis were examined microbiologically and an antibiogram was performed using the disc-diffusion method. Clinical laboratory tests and microbiological examinations were performed in the laboratory block of UMHAT "St.Marina" - Varna. Local therapy with mupirocin and fusidic acid was performed in 111 patients, systemic therapy in 151 patients, 111 of them were treated with combined therapy (systemic and local agents).

**Classical medical and statistical methods** were applied to carry out the research - retrospective clinical and epidemiological analysis, all patients underwent general medical and complete dermatological examination. Statistical discriminant and correlation analysis, parametric and non-parametric methods were used to test hypotheses. A coefficient of  $p \leq 0.05$  was chosen as the significance level at which the null hypothesis was rejected. Data processing was performed using the statistical package IBM SPSS for Windows, ver.25.0.

**The results of their own research and discussion** are published on 49 pages. The data obtained for the selected population are sufficient, therefore I take the results to be reliable.

The epidemiological study and the analysis of the demographic and social structure show that in the territory of Northeast Bulgaria the incidence of bacterial skin infections in childhood is 17.48% of the total pediatric pathology, and gender does not influence the incidence. There was statistical significance in determining the mean age of the patients - 10.1 years ( $p < 0.05$ ), as well as determining the highest incidence of pyoderma in the age 11-18 years for children living mainly in urban conditions (79.2%,  $p = 0.05$ ).

The study of seasonality and risk factors for bacterial skin infections in children showed that bacterial skin infections occur year-round, with a peak in the summer season (48.19%,  $p = 0.21$ ), with risk factors for their development being pathogen carriage in the nasopharynx (27.90%), obesity (20.80%), and atopic dermatitis (18.80%).

The results of clinical data concerning the diagnosis, localization of pathological skin changes and their morphology were the highlight of the study - the most common pyodermas of the skin were impetigo (41.60%), folliculitis (27.30%), ecthyma simplex (11.70%), furuncles (11%)

and perionyxis (7.10%). In 63% of patients, exanthema was localized on the extremities, predominantly exudative lesions (86.40%), followed by erosions (64.30%) and crusts (60.40%). Regarding the etiology of bacterial infections in childhood, the dissertator cited Gram-positive *S. aureus* (41.60%) and MRSA (5.20%). The highest therapeutic efficacy was observed with parenterally administered systemic antibiotic therapy in combination with topical forms of fusidic acid and mupirocin ( $p < 0.05$ ). At the same time, the highest resistance of pathogens to antibiotics was registered to cefazolin - 14,30% ( $p < 0,05$ ), and the lowest to ceftriaxone - 5,20% ( $p < 0,05$ ), while in local forms the sensitivity and resistance of isolates were almost equalized. It was reported that systemic antibiotic therapy was a predisposing factor for the development of allergic reactions in 8.40% of the treated children compared to 2% of the children in the control group who had other systemic treatment ( $p = 0.012$ ).

The results obtained by the author are discussed in the light of the chosen theoretical framework and compared with the results of contemporary studies in the field of infectious dermatology. The discussions made demonstrate sufficient knowledge of the problem by the PhD student Stoyanova, correct reasoning and critical interpretation of the results.

### **3. Contributions and significance of the development for science and practice:**

The dissertation concludes with 6 conclusions that stem from the own research and accurately reflect the results obtained and their analysis. They are described in detail and represent systematic data, some of which are published for the first time in Bulgaria.

I accept the 7 contributions of the dissertation, divided into "original" (1), "scientific and theoretical contributions" (3) and "scientific and confirmatory contributions" (3).

The dissertation is accompanied by a list of scientific production related to the topic, with Dr. Zhenya Stoyanova is the lead author in all the papers. They are 5 in total - 2 publications in Bulgarian medical periodicals and 3 contributions to national scientific forums.

The abstract to the dissertation is 48 pages and adequately reflects the main points of the scientific development.

### **4. Critical notes**

I am pleased to find that the critical remarks I made during the course of the development, related to the structure of the thesis, have been taken into account and the errors have been corrected.

- In places in the text, the Bulgarian translation of 'fusidic acid' is misspelled (pp. 47, 69, 89, 106, 113).
- In the bibliography, sources Nos. 1, 2, 5, 7 and 8, all in Cyrillic, are incompletely spelled - the pages of the articles printed in the respective journals are missing. Sources Nos. 34, 36, 50, 93 are misspelled or incomplete in Latin.
- Critical remarks of a technical nature (spelling errors, periods, commas and spacing) are not substantive and do not affect the scientific value of the thesis.

## 5. Conclusions

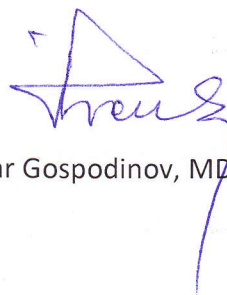
I evaluate positively the dissertation of Dr. Zhenya Stoyanova. It represents a complete scientific work with clearly stated tasks, results and conclusions, which have their own contribution to the development of pediatric dermatology in Bulgaria. My reasons for the positive evaluation are:

- The performed epidemiological analysis of the frequency, demographic and social structure of common bacterial skin infections in childhood, as well as the comparative analysis of pyodermias in children with the general pediatric pathology, which are pioneering for Bulgaria;
- The significant antibiotic resistance found in *S. aureus*, MRSA and *K. pneumoniae* as causative agents of pyoderma in childhood;
- Confirmation of the role of atopic dermatitis, nasopharyngeal carriage of pathogens and obesity as risk factors for the development of purulent skin infections in childhood.

Considering the above I vote "FOR" the award of the educational and scientific degree "Doctor" to Dr. Zhenya Stoyanova Borisova.

22-May-2023

Reviewer:



Prof. Dr. Dimitar Gospodinov, MD, PhD, DSc