

OPINION

by Assoc. Prof. Dr. Klimentina D. Gospodinova, MD, PhD
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Subject: Defense of a dissertation for acquiring the educational and scientific degree "Doctor" (PhD) in higher education 7. Health and Sports, professional field 7.1. Medicine

Author: Dr. Zlatko Dobrev Dimitrov

Doctoral Program: "Dermatology and Venereology"

Topic: Diagnostic value of specific allergy tests in patients with CMPA (Cow's milk protein allergy)

Scientific supervisor: Prof. Nikolay Tsankov, MDq PhD, DSc

Scientific Unit: Clinic of Dermatology and Venereology, Acibadem City Clinic UMBAL Tokuda EAD, Sofia

At a meeting of the Scientific Council of Acibadem City Clinic UMBAL Tokuda on 27.01.2025 (Protocol No. 56/27.01.2025), I was elected as a member of the Scientific Jury and approved by Order No. 15-05-78/19.03.2025 of the hospital management. At the first absentee meeting of the Jury on 20.03.2025, I was selected to prepare an opinion on the procedure for the public defence of the dissertation of Dr. Zlatko Dobrev Dimitrov, MD.

The presented set of materials follows the requirements of the country's regulations.

Relevance of the dissertation topic:

In recent decades, the incidence of allergic diseases has increased, and the prevalence of asthma in childhood at 10% is estimated. Food allergies and anaphylaxis are also increasing, and they are shaping up as a significant public health problem. Following epidemiological trends, the European Academy of Allergy and Clinical Immunology estimates that in about 15 years, more than half of the European population will suffer from some allergic disease. That is why the dissertation topic is relevant and significantly contributes to the practice of dermatologists and allergists in the country.

Structure, characteristics and evaluation of the dissertation :

The dissertation is 146 pages, containing 21 figures, seven graphs and 31 tables. The bibliography includes 307 literary sources, of which four are by Bulgarian authors and 303 by foreign ones.

The literature review analyses the sources cited in the literature, and the problem of "food allergy" is discussed from a historical and contemporary perspective. The current epidemiological data on the prevalence of hypersensitivity to cow's milk and egg proteins are indicated. The epidemiology, pathogenesis and clinic of IgE-mediated allergy to cow's milk proteins (CMP) are examined in detail, and the current applicable diagnostic tests in

allergology to various foods are described. Dr. Z. Dimitrov has provided a broad overview of therapy, including biological and immunotherapy, as well as measures related to preventing and limiting the risk of the manifestation of this type of hypersensitivity.

The goal of the dissertation is formulated and emphasizes establishing the level of tolerance to cow's milk in children based on results from various allergy tests (prick tests, epicutaneous tests, in vitro tests for specific IgE, provocation tests)

The doctoral candidate has set himself **eight tasks** (3 theoretical scientific and 5 applied the sequence, the implementation of which logically leads to achieving the goal.

Materials and methods of the study

The study was conducted in 2016–2022 and included 248 children aged 3 months to 9 years, of which 96 were girls, and 151 were boys, with one child having no gender information. Two age groups were formed – up to 24 months (54.7%) and over 24 months (45.3%).

The accepted clinical methods, allergological in-vitro, epicutaneous and prick tests were applied. The results were statistically processed with the software product SPSS 13.0, using descriptive statistics to describe the indicators, correlation analysis to track dependencies between two or more indicators, and other tests commonly applied in scientific medical studies. To assess the significance level and reject the null hypothesis, a coefficient of $p < 0.05$ is assumed.

The results of our research and their discussion

It was found that the most common dermatological manifestations in both groups of children studied were maculopapular rash (22.7%), followed by urticaria (19.8%), recurrence or worsening of atopic dermatitis (18.6%) and allergic proctocolitis (18.2%). In children under 24 months of age, the most common were allergic proctocolitis (24.4%) and urticaria (24.4%), while in those over 24 months of age, maculopapular exanthema (30.4%), exacerbation of atopic dermatitis with sensitization to cow's milk (19.6%) and angioedema (18.8%). In the manifestation of the most common allergic reactions, no significant difference in the distribution between the sexes was found. In both boys and girls, the most common were allergic proctocolitis, maculopapular rash, exacerbation of atopic dermatitis with sensitization to cow's milk, urticaria, and angioedema. The correlation between the provocation test and the levels of serum-specific IgE is also statistically insignificant. There is significance in the relationship between the combination of the three tests (in vitro tests, epicutaneous and prick tests) and the provocation test results with cow's milk, which is not determined by the type of nosological unit.

The results obtained from the author's research are discussed in the light of the chosen theoretical framework and are compared with the results of contemporary studies in the relevant field. The discussions demonstrate sufficient knowledge of the problem by the doctoral student, correct reasoning and critical interpretation of the results.

Contributions and significance of the development of science and practice:

Dr. Z. Dimitrov has presented his observations in **12 conclusions**, which I accept. They arise from our research and accurately reflect the results obtained and their analysis. They are described in detail and represent systematized data.

The contributions of the dissertation work are 12 in total, 5 of which are original, four are scientific-theoretical, and three are scientific-practical and confirmatory. I accept the contributions the dissertation candidate proposed and fully agree that 5 of them should be referenced as original.

The abstract for the dissertation is 46 pages long and adequately reflects the main points of the scientific work. The list of scientific productions related to the topic is also included here, with Dr. Z. Dimitrov being the lead author in all four publications. There is one participation in a scientific forum with an international presence.

Critical notes and recommendations that do not diminish the scientific value of the dissertation:

- ✓ I consider the spelling of the abbreviation CMPA in the title of the dissertation to be incorrect. It should be borne in mind that not every reader knows the meaning of the abbreviation, which is why the entire given name should be written out. The abbreviation in the work text is accepted.
- ✓ Conclusion #4 could become #1, and conclusions #1, 2, and 3 could be merged.
- ✓ I exclude single and minor typographical errors.

In conclusion:

I positively assess the presented dissertation work. The basis for this assessment is the relevance and originality of the issues, the significance of the set goals and objectives, and the large volume of precisely performed and interpreted research work. The study has a scientific and practical focus and shows the author's severe and profound scientific and scientific-practical interest in this significant topic. The qualities of the dissertation work and the fulfilled requirements for the necessary quantitative and qualitative criteria according to the current regulatory framework in the country and Acibadem City Clinic UMBAL Tokuda", give me reason to vote positively and to propose to the esteemed members of the scientific Jury to award the educational and scientific degree "Doctor"(PhD) to Dr. Zlatko Dobrev Dimitrov, MD.

Date: 22/APR/ 2025
City of Pleven

Reviewer: 
(Assoc. Prof. Klimentina Gospodinova, MD, PhD)