

**To the President of the Scientific Jury
appointed by the Director of NCIPD
with Order No. 512 / 16.12.2019.**

OPINION

by Assoc. Prof. Borislava Georgieva Chakarova, MD, Ph.D., Thracian University - Stara Zagora, Faculty of Medicine, Department of Microbiology and Parasitology

Dissertation thesis for the award of the educational and scientific degree "DOCTOR" Field of higher education: **4. Natural sciences, mathematics and informatics Professional direction: 4.3. Biological Sciences Doctoral Program: Parasitology and helminthology**

Author: Dr. Iskren Tzvetkov Kaftandjiev

PhD form: Self-study

National Center for Infectious and Parasitic Diseases, Sofia. Department of Parasitology and Tropical Medicine

Subject: "CHARACTERISTICS OF IMPORTS AND ASSESSMENT OF THE POSSIBILITY OF MALARIA RECOVERY IN BULGARIA IN CONDITIONS OF GLOBAL CLIMATE CHANGE"

Scientific adviser: Assoc. Prof. Dr. Rumen Nenkov Harizanov, MD, National Center for Infectious and Parasitic Diseases, Sofia. Department of Parasitology and Tropical Medicine

I declare that I have no general publications and no conflicts of interest of another nature within the meaning of para. 1, item 3 of the DR of ZRASRB with the doctoral candidate.

1. General characteristics of the thesis

The dissertation work is structured in accordance with the Rules for the application of ZRASRB at the NCSPD, Sofia. It was developed and implemented in the Department of Parasitology and Tropical Medicine at the NCSPD - Sofia. It is written on 203 pages and is structured in nine chapters. It is illustrated with 43 tables, 86 figures and one application. The bibliography includes 215

sources, 71 of which are in Cyrillic and 144 in Latin. The dissertation is discussed and directed to the defense of an extended scientific collegium of the Department of Parasitology and Tropical Medicine at the NCSPD - Sofia.

2. Relevance of the topic

The topic of the dissertation is very relevant, as it treats one of the most serious human health problems - malaria and the possibility to date for its restoration. The topic is particularly relevant nowadays due to the increased migration of people in the face of global climate change from areas of high endemicity to those in which malaria has been eliminated or is in the phase of preventing its recovery, such as our country. The WHO report for 2010-2017 indicates that malaria cases in 11 countries (India and 10 in Sub-Saharan Africa) account for about 70% of all cases, and the deaths for this period are 275000. Due to their geographical location, Bulgaria is on the path of people migrating from Asia and Africa across the Mediterranean, which poses serious challenges to our medical community and urgent public health challenges.

3. Knowledge of the problem

The last extensive studies on the epidemiological parameters of malaria and the malarogenic potential of our country are by Professor Dr. Peter Petrov from the late 1970s and cover a 60-year period - between 1916 - 1975. The changes that have occurred in the last thirty years in public life and as natural phenomena reflect with a change in the interrelationships in a number of diseases, in particular - with the possibility of malaria recovery in Bulgaria. As an ambitious goal, the author of the dissertation, Dr. Kaftandjiev, under the guidance of his scientific associate professor Dr. Harizanov, sets out to study this possibility, characterizing the current situation with malaria cases in the face of the current global climate change.

Wide-ranging awareness of the issue, the author registers using current scientific literature - 76% of the titles and information in the bibliographic reference have been published since 2000.

The goal stated in the dissertation is clearly stated:

- to evaluate the potential for malaria recovery in Bulgaria;
- to predict the clinical and epidemiological consequences of imports in the face of global climate change.

The tasks that are planned to achieve the goal are 6, they are adequately formulated in structure and include the consistent implementation of the main stages in a research project.

Material and methods

The study covers a 16-year period - from 2000 to 2015, during which 175 cases of malaria were registered, with 2/3 being Bulgarian nationals (n = 123) and the rest foreigners (n = 52). The large number of individuals covered is sufficient to perform mathematical calculations that are statistically reliable. Official accounting and reporting documentation was used; NIMH official data from BAS for the average monthly air temperatures for the period from 2000 to 2015 and those from the dissertation of Professor Dr. Peter Petrov for

the period between 1916 and 1975 for The 28 regions of Bulgaria; data from the Fifth Climate Change Assessment Report of 2013 of the International Commission on Climate Change, as well as the results of laboratory tests on malaria. It works with two software programs - SaTScan and FleXScan. For the mathematical modeling of malaria transmission, Ross - Macdonald and Moshkovsky models were used. A medical-geographical map of Bulgaria has been drawn up, including the data from the spatial analysis of the cases of imported malaria. The materials used and the methods used are up-to-date and the results obtained are appropriately statistically processed.

Results and discussion

Presenting the results of the studies, discussing them and comparing them with the ones found in the open sources of literature show the good analytical approach of the dissertant to the problem and his adequate handling of the scientific literature. As a result of this, the formulated research goals have been achieved. It is estimated that there is a moderate vulnerability to the import of malaria cases on the territory of Bulgaria, with the highest proportion of those with tropical malaria originating in Sub-Saharan Africa. There has been a change in the profile of patients and infectious agents - in recent years, the proportion of Bulgarian nationals infected in malaria-endemic countries is significantly higher than that of foreign nationals who entered our country with malaria. An alarming trend is in the conclusion of the dissertation work - health consequences - clinical complications, incl. deaths were due to delayed diagnosis and etiologic treatment, related to insufficient knowledge of physicians and diagnostic incompetence of laboratory specialists. Last but not least, people's lack of knowledge about the need for chemoprophylaxis when leaving and returning to and from malaria endemic countries is put. It is found that in the last 17 years higher average monthly temperatures have been measured in 19 of the 28 districts in Bulgaria or 2/3 of its territory compared to those between 1916 and 1975. In 12 districts of the country, a reduction in sporulation time is estimated for the three types of malaria parasites - *P. vivax*, *P. falciparum* and *P. malariae* and it is predicted that this would lead to an acceleration of the possible infection rate, more intense transmission. malaria and affecting a larger population. It is specified that on the basis of mathematical formulas and calculations, in the coming years, cases of imported malaria will be registered 1.6 times more likely in clusters: Plovdiv, Pernik, Sofia, Vratsa, Plevan, Turnovo, Sliven, Burgas and Varna , compared to the rest of the country. The analysis of the results helps to reasonably predict the possible damage from the disease when sending contingents in malaria endemic areas.

Contributions and importance of development to science and practice

The conclusions drawn (8) are correctly formulated and are in accordance with the set goals and the tasks solved and correctly reflect the results obtained. The dissertation declares originality, authenticity and correspondence with the objective truth about the obtained results and the formulated contributions and assures of his personal participation in scientific production in the form of documents, publications and references. A total of 10 contributions have been defined: 3 scientific-theoretical, of original nature and 7 of scientific-applied nature, which I approve of in terms of volume and credibility.

4. Evaluation of dissertation publications

Theses related to the dissertation are 5, 2 of which - in impacted journals:

(1) Balkan Med J. 2017; 35: 61-67. doi: 10.4274 / balkanmedj.2017.0167 (IF 1,083); (2) J Infect Public Health 2018; 11: 534-539. doi: 10.1016 / j.jiph.2017.10.010 (IF 1.439); (general IF 2.522).

Participations in scientific forums with reports and communications are 5, 1 of which - abroad. They reflect the results of the studies carried out. Out of a total of 10 publications and participation in scientific forums, in 5 the dissertation is the first author, which shows the commitment and personal contribution to the development of the results and writing of the dissertation.

The abstract for the dissertation is presented in 71 pages and correctly reflects the structure of the dissertation and its main chapters. It is illustrated with 11 tables and 25 figures. A summary in Bulgarian and English is also attached.

In the version of the dissertation work for the acquisition of the Doctor's degree by Dr. Iskren Kafandjiev, my critical remarks and recommendations, presented during the approbation, conducted at the extended panel, were taken into account. Subsequent changes have been made correctly and reflect the scientific approach of the thesis to the problem.

CONCLUSION

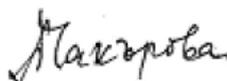
The dissertation shows that the author Dr. Iskren Kaftandjiev possesses theoretical knowledge and professional skills in the scientific specialty "Parasitology and helminthology" and demonstrates qualities and skills for conducting independent research. The adopted methods for dealing with data from retrospective and prospective studies on malaria in Bulgaria and the applied methods for forecasting near and far intervals in changing climate parameters, the results obtained, the significant contributions reflected in the dissertation, give me reason to believe that the research work presented in this way meets the requirements of the ZRASRB and the Regulations for its implementation, adopted at the NCIPD, Sofia.

I am convinced of my POSITIVE assessment of the studies, results and contributions made. I suggest the honorable members of the Scientific Jury to award the Doctorate degree in the field of science and science, Parasitology and helminthology, professional direction: 4.3. Biological Sciences.

Dec 23, 2019

Stara Zagora

Opinion drafted by:



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