

**To the Chairman  
of the Scientific Jury appointed  
by the Director of NCIPD, Sofia  
with order No. 504 / 16.12.2019**

## **OPINION**

**By Associate Professor Borislava Georgieva Chakarova, MD, PhD  
Thracian University – Stara Zagora, Medical Faculty  
Department “Microbiology and Parasitology”**

**Subject: Dissertation thesis for the award of the scientific degree “Doctor of  
Science”**

**Field of High Education: 7. Health care and sports**

**Professional field: 7.1. Medicine**

**Author: Assoc. Prof. Iskra Georgieva Rainova, MD, PhD**

**National Center of Infectious and Parasitic Diseases, Sofia city,**

**Department of Parasitology and Tropical Medicine**

**Topic: Helminthozoonoses (trichinellosis, toxocariasis and echinococcosis) in  
humans - epidemiological indicators, distribution, diagnosis and treatment**

### **General characteristic of the dissertation work**

The dissertation work is written in accordance of the Rules for the application of the Law for the development of the academic staff in Republic of Bulgaria in NCIPD. The doctoral thesis is elaborated and performed in the Department of Parasitology and Tropical Medicine at NCIPD. The dissertation thesis is written on 257 pages and 9 chapters. It is illustrated with 59 figures, 34 tables and an algorithm is formulated. The bibliography contains 427 literature sources of which 88 in Cyrillic and 339 in Latin. The dissertation work has been discussed and aimed at public defense of an expanded scientific college of the Department of Parasitology and Tropical Medicine.

### **Relevance of the topic**

The topic of the dissertation work elaborated from Assoc. Prof. Rainova is extremely up-to-date because of the serious questions posed by zoonoses in medical, veterinary and social aspects. Due to a number of factors determined by climate change, dynamics in socio-economic relationships, restructuring in moral and behavioral norms, zoonoses are expanding their range of distribution, with some increasing morbidity. In most developed countries, cystic echinococcosis is a disease of very low morbidity and prevalence and appears almost exclusively in migrants from endemic countries. Areas with high morbidity are mostly places with insufficient medical and health resources and there the number of patients is too large. Particularly worrying about cystic echinococcosis is the data for

Bulgaria. Our country as a member of EU is permanently ranked first in terms of morbidity and in 2006 half from all registered cases were from Bulgaria. The situation with trichinellosis ranges in different years.

The incidence of trichinellosis in the EU countries is about 0.1 per 100,000 population and over the last 7 years below 0.05 per 100,000 and in Bulgaria in 2018 the incidence is 0.64 per 100,000, with cases accounting for 68, 2% of those in the EU and 5.35 per 100,000 people in 2009, accounting for 54.3% of those in the EU. Toxocariasis as helminthozoonosis in humans is not monitored, therefore the data on the disease in Bulgaria became public because of the research interest of parasitologists in our country. In the context of the above, the topic of the dissertation work of Assoc. Prof. Rainova is extremely relevant, and the work on it is a large-scale scientific research with serious importance for medical science and practice

### **Problem knowledge**

In the dissertation Assoc. Prof. Rainova studies the widespread zoonoses in Bulgaria: trichinellosis, toxocariasis and echinococcosis in three aspects – epidemiological indicators, clinical manifestations and their diagnostic features for 18-year period – from 2000 to 2017.

The data included in the dissertation is representative for the country, and the results of the mathematical processing are statistically significant and represent a reliable characteristic of the problem under consideration. The author registers her professional engagement and up-to-date scientific issues with a comprehensive and accurate literature review on the use of rich scientific literature, WHO documents and other sources of scientific and applied significance. This is evident from the bibliographic reference including 427 titles, 60% of which have been published since 2000.

The goal of the thesis is clearly stated - to study the epidemiological, clinical and diagnostic features of the three helminthozoonoses - trichinellosis, toxocariasis and echinococcosis in the population of Bulgaria for the period 2000-2017.

The tasks that are planned to achieve the goal are 5, they are adequately formulated and by structure include the sequential implementation of the main stages in the research project.

### **Materials and Methods**

The study covers an 18-year period from 2000 to 2017. Official data from the epidemiological cards of the relevant parasitoses, the annual reports on parasitic diseases from RHI in the country and the analysis of parasitic morbidity prepared by NCIPD and NCPHA, the NSI and the Health Fund and own studies were used. For trichinellosis were examined 2068 persons, for echinococcosis - 8157, and 2087 for toxocariasis, as well as 587 healthy persons and risk contingents for determination of seropositivity for toxocariasis in Bulgaria. The selected diagnostic methods are both widely used in practice and modern, mainly used for research purposes, which guarantees their applicability, high specificity and sensitivity. The applied epidemiological methods are appropriate for characterization of

indicators - morbidity and standardized morbidity, prevalence, mortality, Attack rate, extensibility, lethality. The large contingent of persons - 12312, covered over a long period of time - creates a reliable representation of the dynamics of the studied parasitic diseases. The statistical methods are modern, the processing of the data is carried out by a computer program SPSS.

### **Results and Discussion**

The results from the studies, their discussion and comparison with these in the found literature sources are performed in 3 sections respectively to each parasitic disease. As a result, the formulated research goals have been achieved. A trend is found to reduce the incidence of trichinosis and echinococcosis, which is also forecast for the next 5 years. The author reported demographic differences in morbidity - trichinellosis affects the male sex more often, and toxocariasis and echinococcosis – female; seropositivity for toxocariasis is highest in children; the highest is the incidence of echinococcosis in children in the age group 10-19 years and those most affected by trichinellosis are people of active age - between 30 and 39 years old; trichinellosis and toxocariasis are more commonly reported in urban residents and echinococcosis among those in the village. It is emphasized that mortality and lethality in echinococcosis remain high. In the study is shown that the number of outbreaks with wild boar source is greater than those with source domestic pigs, but the differences have not statistical significance. Moreover, a late positivity of serological tests for the diagnosis of trichinellosis is observed - in ELISA specific IgG antibodies are detected on average after 40 days of infection. The author points out that the laboratory tests developed - ELISA IgG avidity and Western blots have sufficient specificity and sensitivity and their application allows early diagnosis for confirmation of trichinellosis and toxocariasis. The dissertation notes the pathogenetic role of toxocariasis in a number of clinical conditions - allergies, eosinophilic syndrome, ocular pathology, etc., but also a significant latent incidence, established on the basis of seropositivity in children and adolescents. It is reported that only 4 areas of the country have no trichinosis outbreaks, while echinococcosis is reported everywhere and in some areas the incidence reaches 15 times higher values than those with the lowest. Despite these alarming facts, it is noted that only 1 in 4 echinococcosis-operated patients underwent postoperative chemoprevention.

### **The contributions and importance of the dissertation work on science and practice**

The conclusions drawn (17) reflect the magnitude of the study and the significance of the results obtained. They are properly worded and are in line with the stated purpose. A total of 11 contributions have been defined - 3 with original character, 5 with scientifically applied, and 2 with applied character, which I accept. In my opinion, especially important for clinical diagnostic practice are:

➤ Elaboration and application of laboratory tests ELISA IgG avidity and Western blot to improve the diagnosis of trichinellosis and toxocariasis.

➤ The development of a laboratory ELISA IgG avidity test for determining the stage of the disease, respectively of the immune response and the time interval during which the disease became chronic in patients with clinical and serological data for trichinellosis and toxocariasis.

➤ The determination of the profile of risk contingents in echinococcosis (persons working with dogs, patients with allergic conditions, women and villagers) is oriented towards organizational measures and can become a basis for development of normative documents for surveillance and control of this socially significant, neglected parasitosis in Bulgaria.

➤ The results of the dissertation can be used as a scientific basis for future programs in order to achieve a lasting reduction in the incidence of helminth infection in the country.

### **Assessment of the publications related to the dissertation work**

The results of the dissertation are published in:

- Monographs in the author's collective - in 5 chapters
- Publications in international and Bulgarian scientific journals with IF - 10, with general impact factor-13, with a total IF – 13,369
- Publications in editions without IF – 12
- Participation in international congresses and conferences with scientific communications related to the dissertation – 9
- Participation in national congresses and conferences related to the dissertation – 23

I highly appreciate the publication activity of Assoc. Prof. Rainova considering the high IF, publication in priority scientific journals and participation in international scientific forums. Citations of her publications (21 of 9 articles) in internationally renowned journals confirm her solid scientific contribution.

Assoc. Prof. Rainova has 4 participations in research projects - 3 national at the National Science Fund and 1 - international with the participation of the Institute of Parasitology in Bern and NCIPD.

**The abstract** is structured in 78 pages and correctly repeats the structure of the dissertation and the main chapters in it.

### **Critical remarks**

I have no remarks concerning serious flaws in the thesis of Assoc. Prof. Rainova. All the results, conclusions, contributions and recommendations made in the dissertation are derived from the years of experience and routine of the author gained in her research and practical activities. I believe that dissertation work should be framed in a monograph to gain more publicity outside the scientific community. The conclusions of the dissertation should be made known to the institutions responsible for public health and to put the problems of neglected parasitic diseases on the agenda.

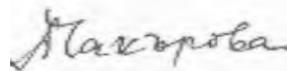
## CONCLUSION

The presented dissertation work is a completed research project of Assoc. Prof. Iskra Rainova MD, PhD, on which she worked long, consecutively, responsibly and conscientiously. It contains scientific and applied scientific results of a beneficial nature. The problems, scope and structure of the dissertation have all the necessary qualities of scientific work for the award of the scientific degree "Doctor of Sciences"

I give my positive opinion on the studies, the results obtained and the contributions made. I suggest the honorable members of the scientific jury to award the scientific degree "Doctor of Science" to Assoc. Prof. Iskra Georgieva Rainova in the scientific specialty "Parasitology and Helminthology", professional field 7.1 Medicine.

3.01.2020

Drafted the opinion:



Assoc. Prof. Borislava Chakarova, MD, PhD