Институт по биология и имунология на размножаването - БАН
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# REVIEW

By prof. Plamen Todorov Todorov, DSc, Institute of Biology and Immunology of Reproduction – Bulgarian Academy of Sciences

**Regarding:** Dissertation on the topic "Etiopathogenesis of partial testicular failure in young men", for the acquisition of the educational and scientific degree "doctor of Phylosophy in Biology" in the specialty "Animal and human physiology", professional field 4.3. "Biological sciences", developed and presented for defense by Georgi Lazarov, PhD student of free form of study at IBIR – BAS.

**Information for the competition:** The dissertation has been discussed and directed for defense by an Extended Sectional Seminar of the Section "Molecular Immunology" at IBIR – BAS. The scientific jury was selected by a decision of the Scientific Council of IBIR (protocol 140/07.10.2025) and appointed by Order 88/08.10.2025 of the Director of IBIR. The first meeting of the Scientific Council was held remotely. I believe that the procedure was followed and all documents for the competition comply with the requirements of the Act on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for the Implementation of the Act on the Development of Academic Staff in the Republic of Bulgaria.

**Information about the PhD student:** Georgi Vladimirov Lazarov received his secondary education at the German Language High School in 1982, and in 1990 he graduated from the Medical Academy in Sofia. He has a recognized specialty in urology since 1994. He works as a specialist urologist-andrologist at First Specialised OG Hospital for Active Treatment "St. Sofia". He has specialized abroad several times. He is a member of national and international professional associations. He speaks German and English. His main interests are in the field of male infertility, erectile dysfunction, hormonal imbalance in men, congenital diseases of the male reproductive system and fetal morphology of the male reproductive system. In January 2022, he was enrolled as a doctoral student in free-form studies at IBIR - BAS.

**Relevance of the topic of the dissertation:** Recently, in connection with an unhealthy lifestyle and harmful habits in young men, complaints of infertility, micturition disorders and erectile dysfunction have become more frequent. There are many studies in the available literature related to the etiology and pathogenesis of infertility and erectile dysfunction, but they remain incompletely understood. In most cases, the occurrence of infertility and erectile dysfunction is associated with the secretion of testosterone. However, in recent years, the claim about the leading role of chronically low testosterone in elderly men has been shaken, and there are no studies in young men. In this aspect, I believe that

the dissertation submitted to me for review is relevant both in a purely scientific and practical sense.

Structure of the dissertation: In terms of volume and structure, the dissertation meets the requirements. All necessary sections are present, the dissertation is 135 pages. It consists of Table of Contents, List of abbreviations, Introduction, Literature review – 25 pages, Aim and objectives – 1 page, Patients and methods – 8 pages, Results – 36 pages, Discussion – 17 pages, Findings, Conclusion, Contributions, List of scientific publications and reports of scientific forums related to the dissertation, List of literature used (Bibliography) and Appendices. There is a good balance in the structure between the individual parts of the scientific work, with the prevalence of the volume of scientific results and their discussion.

The dissertation is illustrated with 23 figures, 15 tables and another 40 tables in the form of an appendix.

*The literature review* is extensive, comprehensively covering all aspects of the problem and providing information that serves the chosen scientific topic and has a contributing character. It includes several subsections. The candidate examines in detail the etiology of androgen deficiency, the various factors affecting testosterone levels. Data on the relationship between testosterone levels and prostatic hyperplasia are presented, methods for diagnosing androgen deficiency, testing testosterone levels, and specialized studies in infertility are comprehensively described.

*Aim and objectives:* The aim of the dissertation is to investigate the relationship between the combination of specific symptoms originating from the genitourinary system (infertility, micturition disorders and erectile dysfunction), suspicious of androgen deficiency, and testosterone levels in men aged 35 to 45 years, in an attempt to determine whether there is a clear discrimination threshold below which they become clinically significant. The aim thus set implies the solution of four main tasks, which are sufficiently precisely formulated.

*Patients and methods:* The dissertation work presented to me for review is based on a large clinical material: 73 patients and 20 controls were personally examined and observed. The author Georgi Lazarov set himself the goal of detecting at what levels of testosterone the combination of infertility, micturition disorders and erectile dysfunction occurs in young men, more precisely from 37 to 45 years of age. This is an original approach that deserves special attention. The methods with which the author conducted his research are modern and adequate for the set goal: the serum levels of testosterone, sex hormone binding globulin were examined and the free testosterone index was calculated as simultaneously, metabolic indicators and those of the sex hormone axis, ultrasound dimensions

of the prostate gland, residual urine, maximum urine flow rate by uroflowmetry, extra- and intratesticular blood flow and blood flow of the a.profunda penis were monitored. The most modern equipment was used, which guarantees the reliability of the results obtained.

*Results and discussion:* The presented results are original and in sufficient volume, have both practical and theoretical significance. They are divided into groups, in accordance with the planned tasks and subtasks.

The author establishes that erectile dysfunction in young men is observed even with a persistently low normal level of testosterone, without changes in the parameters of the blood flow of the a.profunda penis. It has been established that in a group of young men with a combination of specific symptoms originating from the genitourinary system, suspicious of androgen deficiency, deviations in normal testosterone secretion (8.60 - 14.28 nmol/l) are observed for a long period of time, which, although not yet outside the reference values, differ significantly from the same indicators in their peers without symptoms. Changes in hormones from the sex hormone axis and metabolic disorders have been described in this group of patients. An increased volume of the prostate gland, a change in the maximum urine flow rate, ultrasound characteristics and testicular blood flow parameters in these men are also observed. The introduced questionnaire on lifestyle and harmful habits in young men shows for the first time their relationship with the level of testosterone and the appearance of the combination of symptoms originating from the genitourinary system, suspicious of androgen deficiency. This observation, related to the relatively young age of the patients, sheds new light on the study of the pathogenesis of the combination of infertility, micturition disorders and erectile dysfunction.

The excellent statistical processing and presentation of the results in tables and graphs make a pleasant impression. The candidate has shown the ability not only to interpret his own results, but also to compare them with the data obtained by other authors, which testifies to excellent knowledge of the material.

I am categorically convinced that the results are original and there can be no question of any form of plagiarism, which is also confirmed by the reference presented by the scientific secretary of IBIR.

*Conclusions and contributions:* From the conducted research, 4 conclusions have been drawn, which I accept, and 5 contributions have been formulated. The conclusions correctly reflect the obtained results.

*The list of used literature* contains 249 sources, arranged in alphabetical order, of which 9 in Cyrillic and 240 in Latin. They are cited correctly where necessary,

according to the tasks of the dissertation. 51 of the cited sources are from the last 10 years.

Notes on the dissertation:

In places in the dissertation there are blank pages. I also noticed an error in the numbering of the figures - after Fig. 22 follows Fig. 24 (Fig. 23 is missing)

It would be good to provide a link to the cited sources in the bibliography (at least where possible), which would make it easier to find them.

It should be noted that the critical remarks I have made are of a technical nature and in no way belittle the merits of the work submitted to me for review. For me personally, this dissertation is a wonderful example of the science-practice connection and the translation of knowledge in the field of reproductive medicine.

Publications related to the dissertation: The author has three publications on the topic of the dissertation - one in a journal with a quartile Q-3 and two in Q-4, which provides him with the necessary number of points in the relevant direction according to the the Regulations for the Implementation of the Act on the Development of Academic Staff in the Republic of Bulgaria. The results on the topic have been reported at three scientific forums.

The thesis summary (51 pages) has been prepared in accordance with the requirements and reflects all the main results and contributions of the dissertation.

Personal impression of the candidate: I have known Dr. Lazarov since before the period of his doctoral studies at IBIR - BAS. My impressions are that he is a well-prepared scientist, distinguished by enviable diligence, broad scientific interests and high professional ethics, who is respected among his colleagues. I cannot fail to note his responsiveness and ability to work in a team. In a purely professional sense, I have attended a number of conferences where he has given wonderful reports on topics related to male infertility. As an embryologist at an in-vitro center, I have had to work with material obtained by Dr. Georgi Lazarov during surgery on testicles of patients at "St. Sofia" hospital and I am truly impressed by his professionalism (in no case was there contamination of the biopsied testicular tissue or complications after the operations).

Conclusion: The dissertation work submitted to me for review is relevant from a scientific and practical point of view. Its merits, as well as the fulfilled requirements for the necessary quantitative and qualitative criteria according to the Act on the Development of Academic Staff in the Republic of Bulgaria. I strongly propose to the esteemed members of the scientific jury to award Dr.

Georgi Lazarov the scientific and educational degree "DOCTOR" in the specialty "Animal and Human Physiology", professional field 4.3. "Biological Sciences".

Date: 09.11.25

Signature:

/prof. P. Todorov, DSc/