Институт по биология и имунология на размножаването - БАН
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Opinion

Regarding the dissertation work of Georgi Vladimirov Lazarov

Prepared by: Assoc. Prof. Tanya Milachic, PhD, Section "Reproductive Biotechnologies and Gamete Cryobiology" at the Institute of Biology and Immunology of Reproduction "Acad. Kiril Bratanov" - Bulgarian Academy of Sciences.

Subject: This dissertation work was prepared by Georgi Vladimirov Lazarov for the award of the educational and scientific degree "Doctor" in the specialty "Animal and Human Physiology", code 01.06.17, professional direction 4.3. "Biological Sciences" and field of higher education 4. "Natural Sciences, Mathematics and Informatics" with scientific consultants: Prof. Dr. Filip Kumanov, DMSc and Prof. Dr. Stefan Lolov, DMSc, on the topic: Etiopathogenesis of partial testicular failure in young men.

Information on the procedure: The dissertation has been discussed and scheduled for defense at the proposal of the Molecular Immunology Section at IBIR - BAS. The procedure has been accepted and the jury has been approved by the Scientific Council of IBIR and appointed by Order No. 88/08.10.2025 of the Director of the Institute of Biology and Immunology of Reproduction - BAS, for conducting a procedure for the defense of the educational scientific degree "Doctor" of the candidate Georgi Vladimirov Lazarov. The doctoral student is enrolled in a free form of study at the Section of Molecular Immunology, IBIR, BAS.

Analysis and evaluation of the dissertation work:

Structure: The dissertation contains the necessary structural units – content – 2 pages, abbreviations used – 2 pages, introduction (introduction) – 2 pages, literature review – 24 pages, conclusions from the literature review – 1 page, goal and objectives – 1 page, materials (patients) and methods – 9 pages, results and discussion – 36 pages, conclusion - 2 pages, list of literature used (bibliography) – 20 pages, contributions – 1 page, publications on the topic of the dissertation work and presentation of the results at scientific forums and applications in the form of tables – 1 page. The work is 135 pages long with 24 figures, 15 tables and another 40 tables (in the form of an appendix), 249 literary sources. On the topic, the doctoral candidate has made 3 publications and 3 presentations (reports) at scientific forums.

Introduction: The introduction concerns the role of androgens in adult men in relation to the appearance of some specific symptoms such as increased fatigue, loss of muscle mass, insomnia, etc. and when to initiate hormone replacement therapy, as well as the combination of infertility, micturition disorders, and erectile dysfunction in young men.

Literature review: The literature review examines the etiology of androgen deficiency (including age, metabolic disorders, drug use, anabolic steroids), as well as etiology and

pathogenesis of benign prostatic hyperplasia. The diagnosis of androgen deficiency is considered. The current issue of sterility is also touched upon as an important medical-biological and social problem, and in most cases it is due to the so-called "male" infertility and the semen tests related to it are described. Specialized urological tests are described, including ultrasound of the urinary bladder and prostate gland, uroflowmetry, color Doppler ultrasound, etc.

Aim and objectives: The aim of the dissertation is formulated clearly and correctly and represents the need to study the set of specific symptoms originating from the genitourinary system (infertility, micturition disorders and erectile dysfunction), suspicious of androgen deficiency and the relationship with testosterone levels in men age from 35 to 45 years, in an attempt to determine an exact limit below which they become clinically significant. From a formulated goal, the set and corresponding accurately formulated 4 tasks arise.

Materials and methods: In materials and methods or more precisely in patients and methods, the examinations and studies conducted in the andrology office at PSAGBAL "St. Sofia" cover a 6-year period with an initial group of 2281 aged 35 to 45. After completion of the screening procedures, 73 men remain, with the combination of specific symptoms, originating from the genitourinary system, suspicious of androgen deficiency, with patients voluntarily completing the relevant questionnaires and informed consents. Additionally, a control group of 20 healthy men in the same age category with normal BMI, without symptoms of the genitourinary system, was created. An adequate and detailed statistical analysis of the results of the studies was also conducted.

Results and discussion: The results are divided into seven main sections, which include scoring from the first part of the questionnaire, BMI and average testosterone level; results from blood sugar tests, total cholesterol, cholesterol and triglyceride fractions; results of sex hormone axis studies; microbiological studies; seminological studies and ultrasound characteristics of the testicles and Doppler parameters of extra- and intra-testicular blood flow; results of the third part of the questionnaire, prostate volume and maximum urinary flow rate; results from the second part of the questionnaire and blood flow parameters of the deep penile artery. One of the main results regarding subfertility is that the decrease in serum testosterone levels below 14.28 nmol/l for a prolonged period of time and the increased estradiol to testosterone values in young men is a prerequisite for the mild to moderate seminal disorders that are observed in them. Another result regarding BMI is the assumption that in obese men, the etiology is complex, but in general it is a prerequisite for seminal disorders.

Conclusions and contributions: The conclusions are four in numbers and end with a summarized conclusion. In them, in a group of Bulgarian men aged 37 to 45 years, specific testosterone levels were established for a prolonged period of time in combination with symptoms originating from the genitourinary system, suspicious for androgen deficiency, similar to those in adult men with hypogonadism. It is proposed that infertility, micturition disorders and erectile

dysfunction in young men on the one hand, and testosterone levels on the other, in a new terminology: "Lifestyle-related partial testicular failure syndrome in young men". The important role of diagnosing such patients in clinical practice in choosing their therapy in the form of a broad holistic view related to internal medicine is emphasized psychology and urology, which will allow in the future to identify an appropriate hygienic-dietary regimen and to create a correct strategy for the treatment of these men.

The contributions are five and have an original character. For the first time, in young men suspected of having androgen deficiency with long-term deviations in normal testosterone secretion are observed, significantly different from the same indicators in healthy young men; changes in hormones from the sex hormone axis and metabolic disorders in the target group of patients studied are also described; increased volume of the prostate gland is reported, changes in maximum urinary flow rate, ultrasound characteristics and testicular blood flow parameters; an increase in the volume of the prostate gland has been observed as a prerequisite for the occurrence of erectile dysfunction; a questionnaire has been created that assesses lifestyle and harmful habits group in young men with the combination of specific symptoms originating from the genitourinary system.

Literature: A list of 249 literary sources is attached, 46 of which are from the last five years, which contributes to the dissertation work's contemporary and topical character. All cited authors are correctly described and arranged in the appropriate places in the literature review, results and discussion.

Publications and scientific reports related to the dissertation: The candidate has presented three publications in national journals, and in all three he is the first author. The doctoral student has also presented his results at three national scientific forums with international participation, which covers the minimum national requirements for the educational and scientific degree "doctor" according to the Act on the Development of the Academic Staff in the Republic of Bulgaria (ASRB) and the Regulations for its implementation.

In view of the set goal and the obtained results, conclusions and contributions, I find the dissertation work of Georgi Vladimirov Lazarov to be completely satisfactory and up-to-date, both in terms of the problems related to androgen deficiency in young men and their overcoming (in particular the treatment of male infertility), as well as in terms of the scientific nature of the present work.

The presented dissertation meets the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria (ASRB), The Regulations for the Implementation of the Law on the State of the Republic of Bulgaria and the relevant Regulations of IBIR-BAS, as well as the recommended criteria for acquiring scientific degrees and holding academic positions at IBIR-BAS, I give my POSITIVE EVALUATION.

From the above, I propose to the esteemed Scientific Jury to also vote positively and award Georgi Vladimirov Lazarov with scientific consultants: Prof. Dr. Filip Kumanov, DMSc and Prof. Dr. Stefan Lolov, DMSc, the educational and scientific degree "Doctor" in the scientific specialty "Animal and Human Physiology", code 01.06.17, professional field 4.3. "Biological Sciences" and field of higher education 4. "Natural Sciences, Mathematics and Informatics".

19.11.2025.

Sofia

Respectfully:

Assoc. Prof. Tanya Milachic, PhD