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REVIEW

by Academician Prof. Dr. Chavdar Krumov Slavov, MD,

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On the dissertation **" Etiopathogenesis of partial testicular failure in young men",**

with a view to awarding the educational and scientific degree " **Doctor"** in the specialty "Animal and Human Physiology", (01.06.17), professional field 4.3. "Biological Sciences" to **Dr. Georgi Vladimirov Lazarov,** doctoral student in independent training at the Institute of Biology and Immunology of Reproduction "Acad. Kiril Bratanov" - Bulgarian Academy of Sciences, based on Order – 88/08.10. 2025 of the Director of IBIR, by which a Scientific Jury was elected by the National Assembly of IBIR (Minutes 140/07.10.2025).

Dr. Georgi Vladimirov Lazarov is a specialist urologist with an andrological focus and works on an employment contract at PSAGBAL "St. Sofia" (First Specialized Obstetrics and Gynecology Hospital for Active Treatment). He graduated from the Medical University of Sofia in 1990. In 1994 he acquired a specialty in Urology. He specialized in Andrology at the University Hospital in Salzburg (Austria) and at the University Clinic in Sigmaringen at the Medical University of Tübingen, Germany. He is a member of the Bulgarian Urological Society, the German Urological Society and the European Association of Urology. He is fluent in German and English.

His primary research interests are in the field of infertility and hormonal imbalances, as well as erectile dysfunction. dysfunction in men. In recent years, he has been specifically involved in fetal morphology of male individuals.

Enrolled as a doctoral student in independent preparation at IBIR - BAS in early 2022.

The scientific work presented to me for review is structured on 152 pages, of which – a literature review of 29 pages ending with four conclusions from it. The results and discussion are presented on 54 pages. The bibliography contains 249

titles, of which 10 are in Cyrillic. The dissertation work is illustrated with 15 figures; 23 tables and an additional 40 tables, as an appendix.

The problems related to the reproductive health of the nation are current and multifaceted. Infertility and in particular the "male factor" are at the heart of the demographic collapse in our country in recent years. The estimated data for this collapse are alarming. The rate of infertility is increasing drastically, both in females and males (30% for both sexes). The factors for this unenviable statistic are multiple and are part of our modernity and unhealthy lifestyle. That is why any study of the possible causes of male infertility is met with interest and attention.

In this sense, Dr. Lazarov's goal "to investigate the relationship between the combination of specific symptoms originating from the genitourinary system, suspicious of androgen deficiency, and testosterone levels in men aged 35 to 45, in an attempt to determine whether there is a clear discriminatory threshold below which they become clinically significant" has its logic and effect from the results obtained.

To achieve this goal, the author has formulated 4 main tasks concerning the lifestyle of the selected group of men, as well as a comparative analysis between testosterone levels and other metabolic indicators of the sex hormone axis; prostate gland volume and data from the extra- and intratesticular blood flow .

The study covers a period of 7 years (2013-2019) based on the Andrology Office at PSAGBAL, Sofia, and 5765 Bulgarian male citizens, aged 18 to 86, were studied. The current sample from this large volume is 73 men, aged 35 to 45.

The study methodology is a complex of clinical studies (1. Lifestyle Questionnaire; Erectile dysfunction and symptoms of the lower urinary tract and 2. Color Doppler ultrasound of the male genital organs); Laboratory studies including the entire hormonal axis of male individuals; spermatological; microbiological and statistical methods for processing the obtained data, at a critical level of significance $P < 0.05$.

The results obtained regarding Testosterone levels correlate with the criteria used for the patient groups. It is noteworthy that these patients presenting with ED, enlarged prostate gland, Erectile dysfunction and Infertility condition has a T level between 8.60 – 14.28 nmol /l . These results were confirmed with three consecutive blood samples over a period of 45 days.

Interesting results have been noted using the "Questionnaire" and Testosterone levels. They demonstrate the presence of certain deviations in normal Testosterone secretion in young men with specific symptoms suspicious of androgen deficiency.

A negative correlation between testosterone levels and triglycerides has also been found. The latter are in the closest relationship between Testosterone and the lipid status of the patients. Again, in young overweight men, the decrease in T is compensated by Free Testosterone (FT), which depends on the presence of sex hormone binding globulin (SHBG).

Again, variations in the Estrogen / Testosterone ratio were found in this group .

Regarding seminal and instrumental studies, dependencies have been established in reduced testosterone levels below 14.28 nmol /l for a prolonged period of time. Seminological disorders are mostly mild to moderate.

Analysis of the results of the obtained serum T levels and determination of testicular volume and prostate volume, compared to Body Mass Index and Prostate Volume (PV), show the greater importance of T for the initial enlargement of the prostate.

The results of the Erectile Dysfunction study dysfunction in young men demonstrate a complex endocrine disorder, influenced primarily by CNS areas and additionally by the enlarged prostate gland and the appearance of ED, as well as by decreased T levels.

As a result of the results obtained, 4 (four) conclusions were drawn, which convincingly prove the dependence of changes in the body and the appearance of certain symptoms in young men (37-45 years old) with the presence of androgen deficiency in the segment 8.60-14.28 nmol / l Testosterone .

At the end of the dissertation, the author highlights 5 (five) contributions, of which I would highlight:

1. The innovative approach in selecting a group of young men for thorough analysis and follow-up, namely those with T levels between 8.60-14.28 nmol /l ;

2. For the first time in our scientific literature, an analysis of changes in the volume of the prostate gland and testicular tissue in young men, associated with the presence of androgen deficiency, is being conducted.

3. For the first time, a questionnaire analyzing the lifestyle and harmful habits of young men with androgen deficiency and the combination with symptoms of DVT/lower urinary tract/ characteristic of older age is proposed and introduced into practice.

In conclusion, I find the paper presented to me for review, " **Etiopathogenesis of partial testicular failure in young men"** , to be relevant; correctly developed and structured with significant scientific and scientific-applied value.

A very important element of the procedure is the fact that this work was developed under the guidance of such prominent scientists and doctors working in this field, such as: Prof. Dr. Filip Kumanov, MD, and Prof. Dr. Stefan Lolov , MD,.

Considering that the procedure for preparing the dissertation has been followed and knowing the qualities of the dissertation candidate, I am given reason to propose to the members of the Honorable Scientific Jury to award the scientific and educational degree "Doctor" in professional field 4.3. Biological Sciences to Dr. Georgi Vladimirov Lazarov.

29.11. 2025

Sofia

REVIEWER :

(Acad. Prof. Chavdar Slavov, MD)