

REVIEW

by Prof. Dr. Dimitar Konstantinov Gospodinov, MD .
Head of the Department of Dermatology, Venereology and Allergology,
Faculty of Medicine, Medical University – Pleven

Subject: defence of a dissertation for the acquisition of the educational and scientific degree Doctor (PhD) in the field of higher education 7. Health and Sports, professional field 7.1. Medicine

Author: Dimitar Todorov Cherkezov, MD

Doctoral Program: Dermatology and Venereology

Topic: Genital warts in dermato-venereological practice - diagnostic and therapeutic aspects.

Scientific supervisor: Professor Dr Nikolay Tsankov, MD, PhD, DSc

Scientific Unit: Clinic of Dermatology and Venereology, Acibadem City Clinic UMHAT Tokuda EAD, Sofia

At a meeting of the Scientific Council of Acibadem City Clinic UMHAT Tokuda EAD on 06.11.2024 (Protocol No. 54/06.11.2024) I was elected as a member of the Scientific Jury and approved by order No. 15-05-145/19.11.2024 of the hospital management. At the first absentee meeting of the Jury on 20.11.2024, I am appointed as a reviewer in the procedure for the public defence of the dissertation of Dr Dimitar Cherkezov.

The presented set of materials on paper and electronic media is in accordance with the requirements of the regulatory framework in the country and at The Scientific Council of "Acibadem City Clinic UMBAL Tokuda" EAD.

I. Relevance of the dissertation topic:

Genital warts (condylomata acuminata) are considered benign. Proliferations of the skin and mucous membranes in the anogenital area develop after infection with human papillomavirus DNA (HPV). Today, more than 200 genotypes are known. The viral aetiology was established in 1907, and the sexual route of transmission – in 1954. In 1982 Harald Oh Hausen proves the etiopathogenetic relationship of different HPV genotypes with the oncogenesis of anogenital carcinomas - cancer of the cervix, vulva and vagina, penis, and anus. This fact determines the significant social significance of HPV infection, as well as the need for new studies on the frequency of genital warts among the population assessment of the potential risk and effect of the most frequently applied therapeutic procedures in

dermatovenereological practice. That is why the topic of the dissertation is relevant and of significant contribution to the practice of dermatovenereologists in the country.

II. Structure, characteristics and evaluation of the dissertation :

The dissertation is written on 130 standard printed pages – literature review 50 pages; the research methodology (purpose, tasks, materials, working hypothesis, etc.) – 11 pages; the research results – 33 pages; discussion of the results – 8 pages, conclusions and contributions - 5 pages, conclusion – 2 pages, bibliography – 10 pages. It is illustrated with 32 tables and six figures. The bibliographic reference contains 119 literary sources, of which 32 are in Cyrillic and 87 in Latin, quoting respected authors from Bulgarian medicine.

II.1. The literature review is an analysis of the cited literature sources, and the problem of papillomavirus infections is discussed in a historical and contemporary aspect. The current epidemiological data on the spread of the infection, the risk genotypes, the most common age of involvement, and comorbidity with other STIs are indicated. The dissertation has focused on the current clinical manifestation and localization of genital warts and has developed in detail the surgical, incl. laser therapy and conservative treatment of acute condylomas. As an important aspect in limiting the frequency and risk of developing neoplasms, Dr D. Cherkezov has made a broad overview of the prevention of genital HPV infection: primary prevention, which includes vaccination with bivalent (Cervarix[®]), quadrivalent (Silgard[®]), nine-valent (Gardasil 9). A future puzzle is the fact that vaccination is mandatory for all EU countries except Bulgaria and the Czech Republic, where its administration is recommended.

II.2. The purpose of the dissertation is clearly formulated and emphasizes the establishment of the significance and frequency of genital warts in men and to assess the effectiveness and patient satisfaction with the treatment in order to develop and implement diagnostic and therapeutic an algorithm for clinical behaviour and a comprehensive approach to these patients.

The dissertation candidate has set himself **ten tasks**, the sequential implementation of which logically leads to achieving the goal.

II.3. Materials and methods of the study

The study was conducted in the period 1.08.2020 - 01.02.2024 and included 332 men with genital warts who sought medical help from a dermatologist at the SIMP in various medical centres in the cities of Sofia and Kardzhali. The patients were divided into five age

ranges: 3 groups according to social and educational status, two groups according to place of residence and smoking.

Attached are:

- + Documentary method for systematization and analysis of information;
- + Clinical method – history, dermatological status, applied therapy
- + Sociological methods – interview, survey, filling out a DLQI questionnaire, filling out a questionnaire about patient satisfaction with the treatment provided
- + Statistical methods - descriptive statistics, comparative and variance analysis,
- + Method of logical, statistical modelling (with the aim of creating a diagnostic-therapeutic algorithm for patients with genital warts as a standard procedure in practice)

II.4. The results of the own studies and their discussion are published on 41 pages. Analyzing these two sections of the dissertation, it should be borne in mind that in Bulgaria, there are enough studies on HPV infection among women, but the topic is insufficiently studied among men, which is an undisputed original contribution of the work. The data obtained for the selected population are sufficient; therefore, I consider the results to be reliable.

The results show that genital warts in males appear at an increasingly younger age, given the early sexual debut among adolescents. Male circumcision does not affect the prevalence, frequency and course of HPV-genital infection. Condom use is recommended but is not a sufficiently effective preventive measure against HPV. 80% of infections are asymptomatic, and only 10-20% have clinical manifestations - most often condylomata acuminata and less often anogenital carcinomas. Both highly and moderately educated men with good social status, living in large settlements, are affected, as well as patients with low educational status and low health literacy, in whom other STDs are also detected. Men who have irregular and promiscuous sex lives with many different partners are at greater risk, which increases the risk of developing anogenital warts. Virological diagnostics is the leading method of determining the etiological agent, with the most frequently detected and most numerous low-risk types being HPV-6,11,42. High-risk types HPV-16, 18, 31 are detected in nearly 1/3 of the studied population, which determines a potential oncological risk. All therapeutic methods applied in the study are sufficiently reliable, with cryotherapy and THO

emerging as the most effective. However, it should be borne in mind that an important sign for the clinical assessment of the effectiveness of therapy is the presence of relapses.

The results obtained from the author's research are discussed in light of the chosen theoretical framework and are compared with the results of contemporary studies in the field of dermatovenereology and virology. The discussions demonstrate sufficient knowledge of the problem by the doctoral student, correct reasoning and critical interpretation of the results.

III. Contributions and significance of the development for science and practice:

III.1. Dr. D. Cherkezov has presented his observations in **14 conclusions**, which I accept. They arise from our research and accurately reflect the results obtained and their analysis. Described in detail, they represent systematized data, some of which are published for the first time in Bulgaria and are another step in the development of the scientific priority of the Bulgarian dermatological school.

The recommendations to various institutions in the country are logical; they are in the domain of protecting public health and would provoke an update of the currently valid regulations of the Ministry of Health for the diagnosis and prevention of sexually transmitted infections.

III. 2 . The dissertation has eight contributions, 4 of which are original and 4 of a scientific-applied nature. I accept the contributions proposed by the dissertation candidate, and I fully agree that 4 of them should be referenced as original.

IV. The abstract for the dissertation is 52 pages long and adequately reflects the main points of the scientific work. The list of scientific productions related to the topic is also included here, with Dr. D. Cherkezov being the lead author in all four publications.

In conclusion:

I positively evaluate the presented dissertation work. The basis for this assessment is the relevance and originality of the issues, the significance of the set goals and objectives, and the large volume of precisely performed and interpreted research work. The methodology is correctly selected, since similar observations on the frequency of acute condylomas among the male sex in our and world literature are very few or absent. The study has a scientific and practical focus, demonstrates the commitment and competence of the author and shows his serious and profound scientific and scientific-practical interest in this socially significant topic.

The qualities of the dissertation work and the fulfilled requirements for the necessary quantitative and qualitative criteria according to the current regulatory framework in the country and in Acibadem City Clinic UMHAT Tokuda EAD give me reason to vote positively and to propose to the esteemed members of the scientific Jury to award the educational and scientific degree "Doctor (PhD)" to Dr Dimitar Todorov Cherkezov.

Date: 18-Dec-2024

City of Pleven

Reviewer: 

(Prof. Dimitar Gospodinov, MD)