Summary

Analysis of the advancement of phage therapy in Poland

Phage therapy, although still having an experimental status in most countries, has become an important element in the search for new methods for combating bacterial infections. Conducted and completed clinical trials using bacteriophages confirm its dynamic development. Given the growing global interest in phage therapy, a comprehensive synthesis of Polish achievements in this field seems essential, as it has not been done so far. The first articles by Polish scientists on bacteriophages were published just a few years after independent discoveries of phages by Frederick Twort (1915) and Felix d'Herelle (1917). Bacteriophages were used in Poland to treat bacterial infections as early as World War II, and a few years after the war, the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences (IIET PAS) was established in Wrocław, later named after Ludwik Hirszfeld – the Institute's founder and first director. Research on bacteriophages and their therapeutic applications continues at this facility to this day. The nearly 100-year history of bacteriophage research in Poland is rich in events and achievements that have influenced current research trends and phage therapy. The final, and perhaps most important, milestone was the establishment of the Phage Therapy Unit at the aforementioned Institute in Wrocław, where phage therapy has been conducted in humans for 20 years. The Phage Therapy Unit has collected data on the world's largest group of patients who have undergone personalized experimental phage therapy in accordance with applicable legal and ethical requirements. One of the goals of this doctoral dissertation is to analyze the history of bacteriophage research dating back to the 1920s. The second goal is to analyze the current state of knowledge regarding bacteriophages and phage therapy in selected professional and social groups in Poland, based on a conducted survey. The dissertation comprises a series of six thematically related scientific publications – two original articles and two review articles. The series is supplemented by one chapter in a monograph and one editorial article.

The first paper (Żaczek et al. 2020a) focused on the events that marked a turning point in the development of phage therapy in Poland and influenced its current form. It presented the scientific activities of pre-war Polish researchers such as Dr. Jerzy Jasieński and Dr. Bronisława Fejgin, whose work gained international recognition and can now be viewed as pioneering. Other figures in Polish science (including Dr. Irena Lipska) whose publishing activity before and immediately after the war deserves recognition are also

mentioned. The post-war period focuses on Professor Ludwik Hirszfeld – although he did not use bacteriophages for therapeutic purposes, he utilized *Salmonella* phages in epidemiological studies related to the control of typhoid fever. This research was also conducted outside Wrocław at local branches of the National Institute of Hygiene. Undoubtedly, Professor Hirszfeld contributed to the popularization of bacteriophages among Polish researchers and physicians, and his scientific inquisitiveness remains a role model for subsequent generations of young scientists. The following section presents Professor Stefan Ślopek, the second director of IIET PAS, who, during his 31-year tenure in this position, significantly expanded the phage bank and developed phage therapy in various centers in Poland by providing hospitals with phage preparations and providing guidelines for their use. This activity was reflected in numerous English-language scientific publications summarizing the results of treatment with phage preparations from IIET PAS. Research and therapeutic activities continued in the years following Professor Ślopek's retirement from the Institute. However, the real breakthrough came only in the new century. After Poland joined the European Union in 2004 and adapted to new legal and ethical conditions, our country became a leader in phage therapy. This was made possible in 2005, when at the initiative of Professor Andrzej Górski, the Phage Therapy Unit – the first facility of its kind in the European Union - was established. The activities of this center are the subject of the final part of this paper (Żaczek et al. 2020a), as well as the entire article from 2022 (Żaczek et al. 2022a).

The biographies of the first two directors of IIET PAS are supplemented by a chapter in a monograph (Żaczek et al. 2020b) and an editorial article (Żaczek et al. 2022b). The editorial article focuses on Professor Hirszfeld's activities in the first years after the war. Thanks to his determination and scientific passion, he played a significant role in rebuilding academic centers in postwar Wrocław, ultimately leading to the establishment of IIET PAS. His successor, Professor Stefan Ślopek, shaped phage therapy into the form in which it survived for decades. This was accompanied by his intensive publishing activity and the establishment of numerous international contacts. These aspects of his activity are discussed in the aforementioned monograph chapter.

The next paper in this series of publications is an article summarizing the scientific achievements of Polish scientist Dr. Bronisława Fejgin, whose name has rarely appeared in scientific and historical studies on phage therapy (Grzybowski et al. 2021). The presented analysis indicates that she deserves significantly greater recognition and commemoration. According to the available literature, Dr. Bronisława Fejgin is the first Polish scientist to have become interested in the subject of bacteriophages, a fact documented in detail in numerous articles by her. Her work has gained international recognition, as evidenced by both her collaboration with Felix d'Herelle, considered one of the discoverers of

bacteriophages and citations of her achievements in, among others, *Science* – a renowned scientific journal.

The ethical and legal aspects governing experimental therapies, as well as the factors that, following Poland's accession to the European Union in 2004, directly contributed to the efforts to establish the Phage Therapy Unit at the IIET PAS Medical Center, are discussed in a publication devoted to the facility's recent activities (Żaczek et al. 2022a). The publication provides a detailed description of the center's principles for conducting phage therapy in humans, patient qualification criteria, and a therapeutic protocol, along with subsequent amendments. The scientific activity of the employees of the Phage Therapy Department of IIET PAS and its international recognition were also analyzed and summarized.

The last article in the series (Żaczek et al. 2025) comprises a survey conducted between 2022 and 2024 on a sample of 1,098 respondents. The results obtained from this study, along with an optional quiz on knowledge about bacteriophages and phage therapy, led to a detailed analysis of the perception of phage therapy in three groups: individuals lacking expertise on the topics being investigated (i.e., the majority of society), health care professionals, and science and research professionals. For this purpose, based on the responses provided by the respondents in the quiz, a scale consisting of 12 items was created, which – after statistical validation – was used to characterize the study groups and assess the extent to which knowledge about bacteriophages and phage therapy is present in the awareness of Polish society.

As a result of the analysis of available materials, the advancement of phage therapy in Poland over the period of over 100 years was presented, although today it is associated primarily with the activities of IIET PAS in Wrocław, established in 1952. Key figures in Polish science who contributed to its continued development even during the wartime, which currently places Poland among the leaders in phage therapy, were identified. The analysis of the survey results allowed for the identification of the main problems and challenges facing the further development of this treatment method. The most important conclusion from the study is the need to intensify educational efforts, as public acceptance of experimental therapies and the funding of further research are closely linked to public knowledge on the subject. The results indicate that Polish society is open to education in this area.

This doctoral dissertation is in line with the current trend of popularizing phage therapy, and as the first analysis of this type conducted in Poland, it constitutes a starting point for further research in this field.