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The interview with Robert Koch held by Huseyin Hulki and the Ottoman delegation on tuberculin therapy ☆

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ABSTRACT

Robert Koch (1843–1910), who was one of the significant representatives of the golden age of microbiology, claimed to have discovered the tuberculin/vaccine therapy in 1890. During that era, the Ottoman Empire closely followed the important developments in the field of microbiology. For this reason, it was decided that a delegation should have been sent to Germany to observe the lecture "On Bacteriological Research" to be delivered by Koch on August 3, 1890 during the 10th International Congress of Medicine to be held in Berlin. The delegation travelled to Germany and carried out observations and met Koch in the meanwhile. Among the delegation sent to Berlin there was also Dr. Huseyin Hulki Bey, who graduated from the Military School of Medicine in 1885, and could speak French, Greek, Farsi and Arabic. One of the young professors of the medical school, Dr. H. Hulki gathered his memories on the trip to Berlin in a book after his return. In his book published under the title *Berlin Memories* (1892), he related the interview they held with Koch, the various medical centres they visited in Berlin, and the physicians they met there.

This study aims to provide knowledge on the interview held with Koch in Berlin, and its reflections on the Ottoman medicine, in the light of Dr. H. Hulki's memories and other sources shedding light on the relations between Germany and Turkey in the 1890s.

1. Introduction

The famous German scientist Robert Koch's discovery in August 1890 of tuberculin, which he claimed treated tuberculosis, was received enthusiastically in Turkey, as in everywhere else in the world. As soon as the news spread, many scientist travelled to Berlin to learn how tuberculin was obtained, and to assess its therapeutic effects. Among the 2500 physicians, who arrived in Berlin from various regions of the world in order to examine tuberculin therapy, there was also a delegation from Turkey. In this context, among a handful of physicians in whom Koch personally took an interest, and whom he met in person in Berlin, was Dr. Huseyin Hulki along with the other members of the Ottoman delegation. The interview the delegation including H. Hulki held with Koch on 24 November 1890 is interesting in this respect. During the interview, the subject moved on from the impact of tuberculin on the treatment of tuberculosis to studies regarding its trial on leprous patients. After his return to Turkey, H. Hulki published a book bringing together his memories on that trip to Berlin, in which he related the interview in detail [1–3]. Before focusing on this interesting interview that took place in Berlin, it is useful to take a brief look at life of H. Hulki and Koch.

2. Huseyin Hulki (1862–1894)

Huseyin Hulki was an Ottoman physician known for the courses he taught at the military medical school, as well as for his books. Born in Istanbul in 1862, H. Hulki graduated from the Military Medical School in 1885, after which he started to work at the same institution. After working for a while in the physiology department, he turned towards dermatology and venereology. Knowing Arabic, Farsi, French and Greek, H. Hulki taught physiology, and especially dermatology, at the medical school [Fig. 1].

H. Hulki, who had been working for the aim of founding a modern clinic of dermatological and venereal diseases through being the member of the medical school, participated in two medical

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Fig. 1. Huseyin Hulki (1862–1894) [16].

congresses organized in Paris and Vienne: First one was the Syphilis Observee â Constantinople. *Congréss International de Dermatologie*, organized in Paris, August 5–10, 1889, and second one was the Contribution â l'etude de la lepre, une enquete chez les lepreux de l'ile de Metalin. *Second Congress of Dermathology*, organized in Vienna, September 5–10, 1892 [1,4].

He also travelled to Berlin in order to meet Koch and to obtain knowledge on tuberculin therapy. A member of the Ottoman Medical Association, H. Hulki died in 1894, when he was only 32. H. Hulki also published nine books, two of which were translations, during his short life [1,5–7]. [See also List 1]

List 1
Huseyin Hulki's Books.

1. Hulki H. Berlin Hâtırâtı [*Berlin Memoires*]. Istanbul, 1308/1892, Karabet Matbaası, 143 p.
2. Hulki H. Deniz Hamamları ve Kimler Girmelidir? [Swimming Baths and Who Should Enter to Them?] Istanbul, 1310/1892, Mahmud Bey Matbaası, 36 p.
3. Hulki H. Koleraya Karşı Ne Yapmalı? [What Should Be Done Against Cholera?] Istanbul, 1309/1892, Karabet Matbaası, 20 p.
4. Hulki H. Makalât-ı Tıbbiyeden İşret [From Medical Articles: Alcohol]. Istanbul, 1304/1887, Karabet ve Kasbar Matbaası, 100+3 p.
5. Hulki H. Makalât-ı Tıbbiyeden Karın Ağrıları [From Medical Articles: Abdominal Pains]. Istanbul, 1304/1887, Karabet ve Kasbar Matbaası, 50 p.
6. Nurican. Müslümanların Tababete Etdikleri Hidmet yahud Sevâbık-ı Maarifimizden Bir Nebze [Muslims Contributions to Medicine or a Piece of Knowledge Obtained in the Past]. Transl. Hulki H. Istanbul, İstanbul, 1300/1883, Mihran Matbaası, 86 p.
7. Hulki H. Sıyam [Religious Fasting]. İstanbul, 1310/1892, Mahmud Bey Matbaası, 26 p.
8. Nurican. Şafak Sadâları [Voices of the Dawn]. Trnsl. Hulki H. Istanbul, 1300/1883, Mihrân Matbaası, 86 p.
9. Hulki H. Tababet-i Hakîkiye ve Mesâlik-i Bâtıla-i Tıbbiye [Scientific Medicine and the Methods of Magical Medicine]. Istanbul, 1305/1888, Karabet ve Kasbar Matbaası, 44 p.

3. Robert Koch (1843–1910)

Robert Koch, was a famous German scientist known for discovering the *Bacillus anthracis, Mycobacterium tuberculosis* and *Vibrio cholerae*. One of Koch's greatest contributions in the field of microbiology was his introduction of the systematic method known as the Koch postulates, under which he identified the fundamental characteristics of infections. Born in Germany on December 11, 1843, Koch graduated from the Göttingen University Faculty of Medicine in 1866. After practicing as a physician in various cities in Germany, he was appointed to the Imperial Health Office in Berlin, in 1880. Thereafter, he started working at Berlin University in 1885 in order to establish a chair of hygiene. In 1891, he became the director of the Institute for Infectious Diseases [8,9]. Taking a great interest in bacteriology, he laid the foundations of medical bacteriology as a discipline discovering anthrax bacillus in 1876, bringing light its fundamental morphologies called as the "life cycle" and connecting a specific bacterium with a specific disease, at first [8,10].

One year later, in order to identify and compare bacteria, he annunciated his methods developed about staining of bacterial films comprised of fixing and drying them on lamella by means of aniline dyes and photographing bacteria [9].

In 1882, he featly isolated the causative agent of tuberculosis, which was named as "Mycobacterium tuberculosis" in 1883, for the first time. He recognized the new organism in tuberculous lesions by using the serum-based medium in the light of previous knowledge submitted by Jean-Antoine Villemin, who was the French physician proponed that tuberculosis was a transmissible disease [11].

After using the old and new stains in order to observe tuberculosis of tissue, and recognizing that the old stains were influent to absorb the useful chemicals from the air, he estimated the efficiency of ammonia alkalinized the methylene-blue stain. While carrying on his experiments in this direction, he observed the presence of numerous and visible bacteria using caustic potash with the strains, and thus he discovered the tubercle bacillus placed in tuberculous disease [8,10].

Within the context of his works, he traveled to Egypt and India in 1883 when he was the head of the German Cholera Commission. While he was working in India, he discovered the presence of Vibrio cholerae, and detected its contamination by means of drinking water, food and clothing. In Egypt, he studied on fifty patients suffered from "Egyptian eye disease" and detected two kinds of infectious conjunctivitis, thus he recognized the causative organism of the disease, at first [9,12].

Following his works above-mentioned, Robert Koch claimed that he discovered a tuberculin/vaccine therapy for tuberculosis at the International Medical Congress in Berlin, on 3 August 1890, and published this work entitled "A further report on a remedy for tuberculosis" in the same year. However, his claim was confuted by the counter argument that tuberculosis was not treated with tuberculin and even damaged to the patient at the advanced stage [11,13].

Until his claim of having discovered the vaccine (tuberculin) therapy for tuberculosis was confuted, a very widespread and deadly disease in those days, was met with great interest across the world. For this reason, many people travelled to Berlin in hopes of learning the treatment or benefitting from Koch's "treatment method". However, Koch's announcement proved to be too soon, delivered as a result of nationalistic pressures and pecuniary interest and without positive proof. Within a few months, Koch's claim started to be met with the counter-arguments. The subsequent discovery of the toxicity of the substance, and its lack of any therapeutic effects on tuberculosis, inflicted serious damage on Koch's

reputation. However, while tuberculin was not proved useful in treating the disease, it is still used as an important method for its diagnosis. In 1904, Koch resigned from his post as the director of the Institute to travel the world, observing diseases in South Africa, India and Java. Koch was awarded the 1905 Nobel Prize in Physiology or Medicine *"for his investigations and discoveries in relation to tuberculosis*". Koch died on May 27, 1910 in Germany [12–15].

4. The interview with Robert Koch held by the Ottoman delegation

The Ottoman medical delegation was among the 2500 scientists, who travelled to Berlin from all over the world for the purpose of examining the tuberculin therapy introduced by Koch as a cure for tuberculosis, and H. Hulki was a part of the Ottoman delegation. In addition to attending the interview held with Koch, H. Hulki also met Libbrecht, Lankenberch, Virchow and Lister, famous scientists of the time, to benefit from their novel opinions and thoughts. In 1892, after returning to Istanbul, he published his travel memories, which also included the interview held with Koch, as a book entitled "Berlin Memories" [2].

H. Hulki's 123-page book, "Berlin Memories", published in the Ottoman Turkish, comprises six chapters:

1st chapter: Koch, his courses, knowledge about tuberculosis, the effect of tuberculin, its benefits and harms, observations made in various hospitals and clinics,
2nd chapter: The interview held with Robert Koch,
3rd chapter: The microbiology laboratory,
4th chapter: The biochemistry and physiology laboratories,
5th chapter: A course taught by Monsieur Librach [Libbrecht],
6th chapter: The hospitals in Berlin.

The most interesting part of this book, which contains H. Hulki's memories on a period during which important developments in terms of the history of medicine took place, is the second chapter, in which the interview the Ottoman delegation held with Koch on 10 December 1890 in Berlin is related. According to the knowledge obtained from this chapter, when the Ottoman delegation visited Koch's office they saw that many scientists, like them, were waiting for an interview. As time passed, those losing 95 hope in an interview started leaving. As the Turkish group stood up to leave, Koch's assistant told them not to go, and that Koch wanted to meet them however late it was. After waiting for a while in excitement, they 98 entered Koch's modestly decorated study. First, the medal sent by Sultan Abdulhamid II was presented to Koch. This was followed by an exchange of compliments, and began the dialogue between Robert Koch and Huseyin Hulki written below:

R. Koch: "Gentlemen, I kindly request you to test tuberculin therapy on leprous patients in Istanbul and provide me feedback about your findings since there are more leprous patients in Istanbul. Leprous patients apply to the hospital where you work, don't they?"
H. Hulki: "Most of the patients are leprous applying to dermatology ward, at the medical school, where I work. I could test the tuberculin/vaccine therapy at the dermatology ward and inform you about my observations when I return to Istanbul. I wonder whether the tuberculin therapy could be beneficial for the leprous patients like for the patients with tuberculosis?"
R. Koch: "I think, tuberculosis and leprosy have resemblance to each other in many aspects. I hope that my tuberculin therapy would be beneficial on the leprous patients just like the patients with tuberculosis."
H. Hulki: "Have you ever tested it on a leprous patient?"
R. Koch: "No, we have not been able to test it on any leprous patient in Berlin. As you know, leprosy is a rarely-seen disease in Berlin, however I received a letter yesterday from Prof. Kaposi, my friend from Vienna; he stated that he had tested the tuberculin therapy on the leprous patients and observed its beneficial effects. I have already been thinking like he stated! Now, my thought was justified by his letter, of course you would let me know if you can observe its beneficial effects in your tests."
H. Hulki: "There are different forms of leprosy in various parts of the world; could the therapy have the same effect on the patients living in a different climate as in Vienna?"
R. Koch: "I researched into the answers like for your question, I think, effects of the tuberculin therapy are equally beneficial on the patients living in a different climate; different regions."
H. Hulki: "Could you make an inference that the tuberculin therapy is beneficial on the patients in each climate from its beneficial effects on the patients in Vienna? Moreover, now there are various types of disease called as 'leprosy' and their clinical forms are different from each other. For example, is the form of leprosy seen in Sweden same with the form of leprosy seen in Vienna?"
R. Koch: "Many physicians hold opinion with you about your assessment, but I examined the most of the forms under the microscope. I had been researching on leprosy in Sweden, Norway, Vienna and Berlin, and I detected that they had the same form and nature of the disease. I think leprosy has the same form in each climate. Therefore, I would say that the tuberculin therapy could have the same and beneficial effects everywhere."
H. Hulki: "You examined the most of the forms of leprosy widely known throughout Europe under the microscope and found that the form and nature of the disease were identical everywhere. So, do you consider that the form and nature of leprosy have the same features in our climate?"
R. Koch: "In deed, I have never examined the leprosy under the microscope in the East, but I think it also has the same form and nature in your climate. When you return, you would examine the Eastern form of leprosy under the microscope and inform us about the findings."
H. Hulki: "As soon as we arrive to Istanbul, it's our duty to use the tuberculin therapy on the patients with leprosy in our country for the best advantage and to inform you about the findings."
R. Koch: I am very glad to see you here, and if I knew that you were not busy, I would have liked to go on the conversation. I hope we could meet again before you return." [2]

5. Discussion

The period coinciding with H. Hulki's visit to Berlin was one during which very important developments followed each other in rapid succession especially in the field of microbiology, and when these developments were observed by the Ottoman Empire as by the rest of the world. The printed press had developed within the Empire, and physicians, as well as the people, were able to obtain news on the developments in the West through newspapers and periodical medical journals. During this period, when developments in medicine were observed closely also by the Ottoman state, efforts were made to quickly bring innovations to the Ottoman medicine by sending physicians speaking foreign languages to Europe. The travel to Berlin of the Ottoman delegation included Dr. H. Hulki was the proof of these efforts made to follow such developments at close range. The Ottoman delegation examined the latest developments in Berlin, met the famous scientists of

the time, attended their classes, visited hospitals, clinics and laboratories, and returned after obtaining knowledge about the level of development of medicine in Germany. H. Hulki conveyed all of these to us in his book.

However, unfortunately, the subject of tuberculin, which was the main reason for their visit to Berlin, and which was introduced as a drug that was considered very promising with respect to the treatment of tuberculosis, once more came to the foreground, but this time as involved in a series of mistakes. The reason for this was that tuberculin was launched as a therapeutic drug without adequate research. The greatest misfortune in this matter was the fact that Koch had made an announcement on the therapeutic qualities of tuberculin too soon, that is, before sufficient researches had been carried out, due to certain national and economic issues.

After obtaining this knowledge from H. Hulki's book, we were curious about whether a treatment trial involving tuberculin was performed on leprosy patients in Istanbul. In order to obtain knowledge on this subject, we reviewed the medical journals published in Turkey between 1890, the year in which H. Hulki visited Berlin, and 1894, the year of his death, and conducted research in the Prime Ministry State Archives. This review revealed no study or information relating to a trial of tuberculin on leprosy patients in Istanbul. It is understood from the sources that H. Hulki attended the Second Congress of Dermatology that was held between 5 and 10 September 1892 in Vienna and presented a paper on leprosy. However, this paper was not on the treatment of leprosy, but on leprosy in the Ottoman Empire. In his paper, he mentioned that the first leprosaria for leprous patients were founded in the Ottoman Empire, and that Europeans should have followed this example. (Vienna Memories) [16]. We deduced that tuberculin therapy would not have applied on the patients with leprosy in Istanbul, since this scandal arose in the period, when the relations and communication with Europe became closer, about the discovery of tuberculin therapy by Koch after a while travel of the Ottoman delegation to Berlin and the fact that it found place in the Ottoman medical press. In any case, the first ineffective findings about tuberculin theraphy had begun to be published and its adverse effects had been understood since January 1891.

In this context, the interview that the Ottoman delegation made with Koch has importance because it implies the reflection of the discussion on tuberculin theraphy to the Eastern world by means of H. Hulki's memories to disclose an unknown aspect of the discussion.

As for the pathline of tuberculin, although it was considered that it finished in this point, tuberculin skin tests were developed by von Pirquet and Mantoux in 1907; the Bacillus Calmette-Guerin (BCG) vaccine was produced by French bacteriologists Albert Calmette and Camille Guérin through a period of 13 years, from 1908 to 1921; and streptomycin was discovered by Selman Waksman in 1944 as well as anti-tuberculous drugs [17]. Eventhough Robert Koch could not achieve his objective with regard to the use of tuberculin for treatment, it can be used for diagnosis today.

We, as the authors of this manuscript, meet the ICMJE criteria for authorship.

Contributors

Co-author, Gulten Dinc designed the manuscript, researched and reviewed literature, and translated Hüseyin Hulki's book entitled Berlin Hatirati (Berlin Memoires) from Ottoman Turkish to Modern Turkish. The second author, Ayten Arikan, researched and reviewed the literature and contributed to writing the manuscript. Both of the authors were interested in analysis and interpretation of data based on literature. Both of the authors approved the final the version of the manuscript to be submitted.

Conflicts of interest

The authors declare no conflicts of interest in this manuscript.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.03.038.

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