

The collaboration of Maurice Nicolle et Adil Mustafa

The discovery of Rinderpest agent

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SUMMARY

The earliest relationship between Turkey and European countries in the veterinary field was initiated with the establishment of the first veterinary school in Turkey in 1842. Through the 19th and 20th centuries, many scientists, researchers and specialists from different part of Europe came to Turkey to contribute educational activities, institutionalization, organisation and legal restructuring of services related to veterinary medicine. One of the prominent results of these co-operations is seen in the researches of Dr. Nicolle, founder of the Imperial Institute of Bacteriology (1894), and Military Veterinarian Adil Mustafa, founder of the first Veterinary Bacteriology Institute in Turkey. They first succeeded in preparing therapeutically rinderpest serum and then discovered the rinderpest agent as filter-passing virus. This discovery, which was the success of joint effort of the veterinary and medical sciences, as well as Turkish-French collaboration, made Nicolle's and Adil's names immortal in veterinary and science history. This review deals with the historical roots of veterinary bacteriology in Turkey and the international collaboration of Adil Mustafa and Maurice Nicolle, resulted the discovery of rinderpest agent.

Key-words: History, rinderpest, Maurice Nicolle, Adil Mustafa, Turkey.

RÉSUMÉ

**La collaboration de Maurice Nicolle et Adil Mustafa.
La découverte de l'agent de la peste bovine.**

La première relation entre la Turquie et les pays européens dans le domaine vétérinaire a été commencée avec l'établissement de la première école vétérinaire en Turquie en 1842. Aux 19^{ème} et 20^{ème} siècle, beaucoup de scientifiques, chercheurs et spécialistes des différentes parties de l'Europe sont venus en Turquie pour contribuer aux activités éducatives, à l'institutionnalisation, à l'organisation et à la restructuration légale des services liés à la médecine vétérinaire. Un résultat important de cette coopération a été observé dans les recherches de Dr. Nicolle, fondateur de l'institut impérial de la bactériologie (1894), et d'Adil Mustafa vétérinaire militaire, fondateur du premier institut vétérinaire de la bactériologie en Turquie. Ils ont réussi, pour la première fois, à préparer thérapeutiquement le sérum de la peste bovine et de plus ont découvert que l'agent de la peste bovine est un virus filtrable. Cette découverte, qui était le succès de l'effort commun des sciences médicales et vétérinaires, aussi bien que la coopération Franco-Turc, a fait immortels les noms de Nicolle et d'Adil dans l'histoire du médecine vétérinaire et de la science. Cette revue traite les racines historiques de la bactériologie vétérinaire en Turquie et la collaboration internationale d'Adil Mustafa et de Maurice Nicolle qui a provoqué la découverte de l'agent de la peste bovine.

Mots-clés : Histoire, peste bovine, Maurice Nicolle, Adil Mustafa, Turquie.

Introduction

Rinderpest is certainly one of the epizootic diseases for which the most historical information exists [6]. It has long been associated with wars and invasions where there is uncontrolled movement of people and their cattle. Invasion by the Huns into Europe in the late 4th century resulted in an outbreak of a highly contagious disease of cattle which was clearly identified for the first time as rinderpest by the Latin writer Severus Sanctus Endeleichus [3]. During the second half of the 18th century some European countries focused on the prevention of rinderpest since the continent was under siege from the disease threatening the future of the animal population. Massive European outbreaks in this century led to the establishment of the first veterinary school in Lyon in

1762. When Bourgelat succeeded in creating a scientific veterinary profession, students from almost all European countries were sent to his school [8]. After this historical event, 25 veterinary schools were also established in the Western Europe until the end of 18th century [11]. Although the eastern part of Europe, where animal diseases particularly the rinderpest prevailed and caused serious economic losses, was within the borders of the Ottoman State, the Ottomans were not interested in this event for 80 years. Following the foundation of the first veterinary school (1842) in the Ottoman State, both veterinary teachers and researchers from Europe were invited to the State and veterinary students were sent to European Countries for education and specialisation in different branches of veterinary science [8]. One of the prominent results of these scientific cooperations is seen in

the collaboration of Dr. Maurice Nicolle and Military Veterinarian Adil Mustafa. This study is aimed at providing holistic information on these two scientists and the discovery of rinderpest virus within the context of Turkish Veterinary Bacteriology.

The historical roots of veterinary bacteriology in Turkey

One of the most important and influential periods of the history of Turkish veterinary medicine comprises the beginning and development of bacteriology in Turkey [9]. As it is known, the discovery of rabies vaccine by L. Pasteur received world wide attention. The Sultan of the Otoman Empire was interested in this scientific event and decided to send a health mission consisting of Dr. Zoeros Pasha, the president, Dr. Huseyin Remzi and Veterinarian Hüseyin Hüsnü, to Paris in June 1886 (Fig. 1). Zoeros Pasha relates their studies in Paris, as well as his idea on the novelties he observed there and comments on the advantages of them in case of application in the Empire, in his report dated December 29th of 1886, prepared on his return from Paris. Zoeros Pasha and Hüseyin Hüsnü Bey learned the vaccination practice, attending Pasteur's Laboratory. Zoeros Pasha studied bacteriology for three months and Huseyin Remzi attended the laboratory of "Jardin des Plantes" in order to do some zoological researches. When they returned home the Rabies Vaccine Laboratory which later became the Rabies Hospital was opened in Istanbul in 1887 and Dr. Zoeros Pasha became the first director of this establishment [9, 21]. In this laboratory the rabies vaccine was produced and applied successfully. Dr. Zoeros and Pasteur corresponded continuously on the quality and the efficiency of the vaccine [20]. As a result of this friendly and scientific cooperation, some students from both Medical and veterinary schools were sent to France for education by the end of 1890's. On the other hand, Professor Chantemesse from the Institute Pasteur was invited to Turkey to participate in the control programme of a human cholera epidemic which broke out in 1893. He stayed there three months. Before going back to Paris, he reported the necessity of setting up a bacteriology laboratory in Istanbul and recommended Dr. Maurice Nicolle from the Institute Pasteur as the Director for this establishment [2, 7, 10, 18].

Maurice Nicolle & Adil Mustafa Sehzadebası

Maurice Nicolle (Fig. 2), brother of Professor Charles Nicolle (1866-1936), Nobel Prize owner, was born in Rouen on March 1, 1862, where his father, Eugène Nicolle, was medical doctor at the municipal hospital, as well as a professor of natural history at the École des Sciences et des Art. He received, together with his brothers, early tuition in biology from his father and, after education at the Lycée Corneille de Rouen, he entered the local medical school. He has improved himself on anatomopathology by having his internship near



FIGURE 1: Turkish Health Mission in Paris (1886).



Figure 2: Maurice Nicolle (1862-1932).



Figure 3: Adil Mustafa (1871-1904).

Professor von Kolliker at Germany and submitted his dissertation named "Contribution à l'étude des affections du myocarde: les grandes scléroses cardiaques" in 1890 [1].

After his graduation, Nicolle started to conduct the preparatory of microbiology courses which W. Haffkine had represented at the Institute Pasteur, he developed the staining technique of bacteria cilia, named *Nicolle-Morax* technique, together with V. MORAX in 1893 by studying the microorganism on the staining techniques [1]. Upon the proposal of A. Chantemesse and the request of the Ottoman Sultan Abdulhamid II, Nicolle came to Turkey at the end of 1893, founded the "Imperial Institute of Bacteriology" in Istanbul in 1894 and was appointed to the directorship of this Institute. In the meantime he also begun to carry the bacteriology instructorship out at the School of Medicine which was the unique Medical School in Turkey during that period [1, 9, 10]. Regarding the Institute Pasteur as a sample, he determined the working areas and principles of the Imperial Institute of Bacteriology which is the third of the 31 laboratories formed in the world by the Pasteuriennes. Here, three months bacteriological courses, of which Nicole has prepared the program in accordance with his tutor Dr. Emile Roux's courses, were carried out not only for the students of medical and veterinary schools, but also for physicians and veterinarians. At the same time this unit was a kind of research center both for human and animal diseases [9, 12, 22].

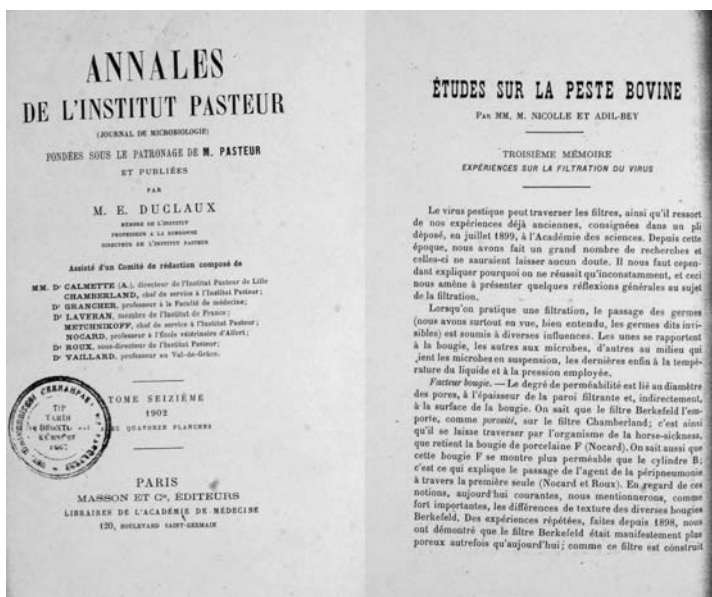


Figure 4: The article, announced the discovery of Nicolle and Adil Mustafa (1902).

In the 8th International Congress of Hygiene and Demography held in Budapest on September, 1894, the announcement of positive results of anti-diphtheria serum therapy in diphtheria cases that applied by Emile Roux and his colleagues at Paris Children Hospital by Roux had had great attention all around the World. To send Nicolle to France for a short time by Sultan Abdülhamid II in order to learn how this serum was prepared had connected the ways of Maurice Nicolle and Adil Mustafa, the brilliant student of NOCARD [12].

Adil Mustafa (Fig. 3), better known as Adil Bey, was born in Istanbul on June 11, 1871. Following his high school education, he entered the Military Veterinary School in 1889. A year later, through an examination, he was sent to *Ecole Nationale Vétérinaire d'Alfort*. Due to his successful exertions here, he was decorated with a silver medal given by French Ministry of Agriculture and achieved to be both the student and preparator of the prominent veterinary pathologist and bacteriologist Edmond Isidore Étienne Nocard. He was graduated from Alfort in 1895. As soon as he returned to Turkey, he joined the teaching staff of the Epidemiology and Meat Inspection Department of the Military Veterinary School [1, 5, 10].

Adil Mustafa, learned to prepare anti-diphtheria serum near NOCARD during his student time in France, was elected as the assistant by M. Nicolle, acquainted with him from Paris, to produce anti-diphtheria serum at the Imperial Institute of Bacteriology. Shortly after starting to work here, he ensured the production of the diphtheria antitoxin serum which is the first native serum in Turkey [1, 5, 9, 10]. Besides diphtheria, cholera, pasteurellosis, tuberculosis and glanders, rinderpest was regarded as an important research field at the Imperial Institute of Bacteriology. Regarding the utilizable character of the serum that Nicolle and Adil could experimentally produced against rinderpest, the mass production of rinderpest serum had been started in the Institute beginning from the year 1899 [22].

Nicolle and Adil obtained very original results from the researches on rinderpest and published related articles in



Figure 5: Adil Mustafa with some members of Nicolle Family in the Institute Pasteur during his visit to France (from the view of Maurice Nicolle).

Annales de l'Institut Pasteur in 1889, 1901 and after Nicolle's return to France in 1902 respectively [14, 15, 16]. In the article published in 1901, it was determined that the virulence differences of rinderpest virus in various cattle breeds and the incubation periods had been tested. According to the results, it was understood that the steppe breeds were more resistant to the virus than the native black [Anatolian Black] cattles and breeds imported from Europe and the incubation period in the native black's was a day more longer from the European breeds [15].

With their article published on *Annales de l'Institut Pasteur* in 1902 (Fig. 4), Adil and Nicolle announced all the world that the rinderpest disease was caused by a filter-passing virus and got privilege status in classical medical literature. In this article, it was explained that they actually carried the experiments of this discovery out nearly three years before and sent some information about these practices to the Academy of Sciences in France in 1899. But, they could not get same results in the repetition of their examinations that is why they could not announce this discovery in that period. Afterwards they recognized that these differences could be stemmed from some difficulties occurred during filtration process. After overcoming these troubles, there was no doubt about the agent of the rinderpest so it was time to announce it [16].

On the other hand according to French Scientist J. Blancou, "these two authors had great difficulty in gaining acceptance for their discovery. They were contradicted by Yersin, who held that rinderpest was bacterial, on the pretext that it was clinically similar to human plague" [6].

This discovery was as the second of its kind, after the foot-and-mouth disease which was the first animal disease caused by a filter-passing virus proved by F. Loeffler and P. Frosch in 1897 [19, 22].

According to Anne Marie Moulin [13], Dr. Nicolle, who had all the scientific, financial and administrative authorities about his job in accordance with his contract, had estranged both his Ambassador and the Sultan, as he had lodged com-

plaints against the Ottoman authorities to the Institute Pasteur as some of his requests for the Institute had not been responded and he had refused the request of Kaiser Wilhelm II, who had come to Istanbul in 1898, to go around the Bacteriology Section. That is why his authorities had started to be distributed and with the request of Dr. Roux, who regarded Nicolle's complaints, Nicolle resigned on July 1901 and returned to the Institute Pasteur in August. However, both the scientific collaboration and friendship of Nicolle and Adil Mustafa had lasted until the death of Adil Mustafa (Fig. 5). As a matter of fact, Nicole and Adil Mustafa, who had implemented significant studies on malleus and piroplasm besides rinderpest in the Imperial Institute of Bacteriology, published their articles on these studies after Nicolle's return to France [1].

The prominent Turkish Bacteriologist Professor E. K. Unat underlined that Nicolle and Adil also carried their researches on variola vaccinae and demonstrated five year before Negri that the agent of it was filterable. But the related article of this research could be published in 1906 - two years after the death of Adil Mustafa [19]. In this article, Nicolle and Adil informed that following pancreas digestion they filtrated variola vaccine from Berkefeld filters and determined that the filtrate was virulent. In the same publication, the use of trypsin for the digestion of tissue materials, was first suggested by them too [17].

After Nicolle's departure, the veterinary bacteriological laboratory was separated as an independent department from the Imperial Institute of Bacteriology and Adil Mustafa was appointed as the founder and Director of this new department called "Veterinary Bacteriology Institute". At the same time he became the Director of the Civillian Veterinary School which was founded in 1889. He continued his research and teaching activities although he was suffering from tuberculosis during these years. When he passed away in 1904 he was only thirty three years old [4, 5].

On the other hand, after his resignation in 1901 Nicolle returned to France and begun to carry out both his studies and research activities with the prominent microbiologists of that period and the instructorship for some famous students such as E.Césari, J.Magrou ve E. Pozerski in the Institute Pasteur. He was appointed as chief of the microbiology courses of which R. Legroux was the preparator between the years 1910-1914. He accidentally was inoculated with malta fever in 1916 and treated by L. Cotoni then had his first paralysis of the right side of his body. All of these conditions did not prevented him from his studies. He continued his scientific activities and as one of the authors he completed the second edition of the book "Éléments de microbiologie générale". He had to halted all his scientific activities after the second paralysis, and passed away in 1932 in Paris [1].

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