Paul Ambroise REMLINGER: a Pasteurien in Turkey and his studies on rabies

B. MELİKoğlu¹, R. T. BAYAĞAÇ GÜL²*, T. ÖZKUL³

¹Department of Veterinary History & Deontology, Veterinary Faculty, Ondokuz Mayıs University, 55139 Samsun/TURKEY.
²Department of Veterinary History & Deontology, Veterinary Faculty, Ankara University, 06110 Ankara/TURKEY.
³Department of Veterinary History & Deontology, Veterinary Faculty, Uludag University, 16059 Bursa/TURKEY.

*Corresponding author: tamaybasagac@gmail.com

SUMMARY

Although the science of modern microbiology started in Turkey at the beginning of the 20th century, one of its roots historically dates back to the foundation of the first medical and veterinary schools in 1827 and in 1842 respectively and the other to the discovery of the rabies vaccine by Louis Pasteur in 1885. After this discovery, a health mission was sent from Turkey to Paris to learn anti-rabies immunization techniques. When the mission returned, the Rabies Vaccine Laboratory was founded in Istanbul in 1887 and the head of the health mission, Dr. Zoeros Pasha, became the first director of this establishment. After him, this laboratory was successively directed by three Pasteuriens, A. C. Marie, P. A. Remlinger and P. Simond till the beginning of World War I. Dr. Marie’s successor, Paul Ambroise Remlinger, carried out remarkable studies on rabies during his directorship between the years 1900-1910 and became a world-class expert on this subject. This review deals with Remlinger’s studies on rabies from the point of view of the Istanbul of 1900’s.

Keywords: History, Rabies, Pasteur, Remlinger, Turkey.

RÉSUMÉ

Paul Ambroise REMLINGER: un Pasteurien en Turquie et ses études sur la rage

Bien que la microbiologie moderne ne soit née en Turquie qu’à la fin du XIXe siècle, l’origine de cette science remonte à la fondation de la première écoles de médecine humaine (1827) et de médecine vétérinaire (1842), et à la découverte du vaccin de la rage par Louis Pasteur en 1885. Après cette découverte, une mission d’étude sanitaire fut envoyée à Paris pour apprendre les méthodes d’immunisation antirabique. C’est au retour de cette mission, en 1887, que fut fondé à Istanbul le Laboratoire de la vaccination antirabique et le chef de mission, le Docteur Zoeros Pasha, en devint le premier directeur. Après lui, ce laboratoire fut successivement dirigé par trois Pasteuriens : C.A. Marie, P.A. Remlinger et P. Simond jusqu’au début de la Première Guerre Mondiale. Le successeur du Docteur Marie, Paul Ambrose Remlinger effectuait de très remarquables études sur la rage pendant ses fonctions de directeur entre les années 1900-1910, et devint un spécialiste mondial de cette maladie. Cette revue, replace les études de Remlinger sur la rage dans le contexte de l’Istanbul des années 1900.

Mots clés : Histoire, Rage, Pasteur, Remlinger, Turquie.

Introduction

In the 19th century, canine or street rabies was a scourge everywhere in Europe. Fear of rabies, related to the mode of contamination and the absence of any effective treatment, was almost irrational. Patients commit suicide, or were killed by others when bitten by a dog believed to be rabid [15]. Louis Pasteur began to work on rabies during the last quarter of this century. He first succeeded in stabilizing the rabies virus by multiple transmissions from one species to another, and starting in 1884, presented the successful results of a pre-exposure rabies vaccination experiment in dogs. Encouraged by some physicians, namely by Doctor Jacques-Joseph Grancher, Pasteur then thought that the post-vaccinal immunity could be effective even after the bite, and could therefore be proposed as a post-exposure treatment in human beings [7]. Pasteur took the step in 1885 and obtained his first success in humans with the vaccination of a 9-year-old child, Joseph Meister, who suffered from multiple deep bites. During 13 days, Joseph Meister received one injection of a more and more virulent rabbit medulla homogenate, and he survived. Three months later, Pasteur repeated the experiment on a young shepherd, Jean-Baptiste Jupille, severely bitten by a rabid dog. On 26th October 1885, he presented the promising results of his treatment against rabies in humans to the French Academy of Sciences. From then on, patients bitten by rabid animals flocked to Pasteur’s laboratory. On 1st March 1886, Pasteur presented the results of the post-exposure treatment of 350 men or women to the French Academy of Sciences. A few months later, he reported the results of 726 treatments. In the memorable meeting of 1st March 1886, Pasteur concluded: "Rabies prophylaxis after a bite is justified. There is cause to create a rabies vaccine establishment" [1].

The Sultan of the Ottoman State, who was extremely interested in all these scientific events, sent a health mission, consisting of two physicians and a veterinarian, to Paris to learn how the method of the vaccination of rabies was practiced [5, 16, 18, 21]. The mission, who arrived in Paris on 6th June 1886, offered on behalf of the Sultan a special medal to Pasteur as well as a 10,000 F donation for the foundation of a new Institute. In Paris, the mission studied the preparation of rabies vaccine and other microbiological techniques [19, 22]. Upon their return, The Rabies Vaccine Laboratory (Fig. 1) – the first known bacteriology laboratory in the East which later became the Rabies Hospital – was founded in 1887 and Dr. Zoeros PASHA, the head of the health mission, was appointed as its first director [5, 22]. After him, this foundation was directed by three consecutive “Pasteuriens”: Dr. Auguste C. MARIE (in 1899 and 1900), Dr. Paul Ambroise REMLINGER (from 1900 to 1910) and Dr. Paul SIMOND

REMLINGER’S ISTANBUL YEARS AND STUDIES ON RABIES 375

(from 1910 to 1914) respectively [16, 18]. The purpose of this article is to review Dr. REMLINGER’s scientific achievements at the Rabies Vaccine Laboratory in Istanbul and to describe his original findings on rabies.

Paul Ambroise REMLINGER (1871-1964)

Dr. Paul Ambroise REMLINGER (Fig. 2) was born on December 29, 1871 in Bertrange (Moselle). Once he received his medical degree from the École du Val de Grâce, he focused on the field of microbiology and started to work at the bacteriology laboratory of this school in 1893. Three years later he was appointed as head clinician in the bacteriology laboratory established by the French Army in Tunisia [8, 18]. Upon the proposal of the well-known microbiologist Dr. Emile ROUX, he was appointed to directorship of the Rabies Laboratory in Istanbul in 1900. In the meantime, he was also appointed as assistant director at the Imperial Institute of Bacteriology, headed by another Pasteurien Maurice Nicole [12]. During those times, because of some bureaucratic issues, as well as because of the vast hinterland of the Empire that extended from Asia to Europe and Africa, and inadequate transportation facilities, it was quite difficult for the patients, exposed to dog bites, to reach the Rabies Laboratory in Istanbul. Remlinger knew that, and was also aware that previous Pasteurien working in Istanbul had faced some difficulties due to politic intrigues and negative attitudes towards foreigners. Despite all these negative circumstances, he agreed to work in Turkey, and arrived in Istanbul in October 1900. He was only 29 years old and not really familiar with rabies [4, 12]. When he was asked to teach rabies courses to medical students, he got a good opportunity to improve his knowledge on this disease [12, 18].

Remlinger’s investigations on rabies

Remlinger got rapidly acquainted with the relevant literature on rabies, and started his experimental work and post-exposure treatment of rabies at the Laboratory. When Nicolle resigned from the Imperial Institute of Bacteriology in 1901, besides his duty at the Rabies Laboratory, Remlinger was also appointed to directorship of this Institute (Fig. 3) and then he focused even more on rabies research [9].

In 1902, Dr REMLINGER, Dr. Rifat BEY (Fig. 4) and Laboratory Assistant Hamdi Efendi made a quite original experiment. They mixed a fixed rabies virus homogenate with a rather virulent culture of the fowl cholera agent (*Pasteurella multocida*), put the mixture through a Berkefeld V Filter and this mixture was then inoculated intracerebrally in rabbits. While the absence of *Pasteurella* among the inoculated animals confirmed the success of filtration, their death from rabies after displaying paralysis symptoms within

![Figure 1: The Rabies Vaccine Laboratory located next to the Medical School (1887).](image1)

![Figure 2: Dr. Paul Ambroise REMLINGER](image2)

![Figure 3: The official document on Remlinger’s appointment to directorship of the Imperial Institute of Bacteriology (1901).](image3)
8-10 days made clear that the rabies agent could pass the Berkefeld V Filter. Remlinger went on to repeat the same experiment by using both fixed and street viruses, and filtering the agent through less and less permeable Berkefeld and Chamberland filters, and was thus able to demonstrate that the rabies virus could pass through the porcelain filters [10, 11]. He therefore not only confirmed Pasteur’s hypothesis that the rabies agent was a filterable virus, but at the same time demonstrated that it was not a parasitic protozoa, as once claimed by the well-known Italian pathologist and microbiologist Adelchi Negri, who discovered the intraneuronal inclusions (Negri bodies) which represent specific features of rabies and provided a histopathological diagnostic criterion for such infection [2, 3]. This discovery was published worldwide through the articles, published in the Compte-rendus de la Société de Biologie (Fig. 5) and the Annales de l’Institut Pasteur (Fig. 6) in 1903.

On 6 April 1903, Remlinger was requested by a decree from the Sultan to vaccinate post-exposure 12 oxen and 20 buffaloes bitten by a rabid dog. Until this time, such treatment had been administered only to humans, as most of animals were treated before exposure. Although Remlinger was aware of that, he vaccinated the animals and 62% of the most seriously wounded animals died despite the treatment [12, 19]. This does not come as a surprise, because we know now that, even using the best modern rabies vaccine, the post-exposure treatment is never 100% effective in animals except when associated with serotherapy [17]. Remlinger then tried to improve the post-exposure treatment in animals and obtained promising results. On this occasion, he observed that mice and rats were susceptible to rabies and that they could even be infected subcutaneously. He also warned that bites of these rodents could possibly contaminate human beings [12, 19]. This receptivity of rodents to rabies has been confirmed later in rare instances, and the World Health Organization therefore is considering now that these animals do not serve as reservoir of the disease in nature [20].

In 1905, Remlinger sent a questionnaire to all institutes working on rabies, in an attempt to collect data about some paralysis incidents which were reported after the injection of rabies vaccine. At that time, such incidents were not common due to the encephalitogenic activity of some brain tissue vaccines produced in adult animals. Nevertheless, he found a little evidence of these incidents, only in a few local

---

**Figure 4**: Dr. Rifat BEY

**Figure 5**: Société de Biologie (1903).

---

**Figure 6**: Annales de l’Institut Pasteur (1903).
articles on this subject, and he concluded that post-vaccinal paralysis was a rather event, occurred rarely. His publication was also regarded as important and received a large attention [19]. Remlinger also discovered, in 1907, that the rabies virus could be shed for a while in the saliva of dogs who recovered from the disease [8, 12, 19]. During the ten years spent in Istanbul, he successfully treated 6709 of a total of 6808 patients exposed to rabid animals [6]. He also published approximately 50 original articles on rabies [18]. Following all these successful works, he left Istanbul in 1910, and was appointed to Tanger Pasteur Institute [4, 8]. He devoted the rest of his career to further studies and publications on rabies [4, 8, 13, 14, 18].

Twenty-four years after his departure from Turkey, he published a brochure (Fig. 7) in which he reported all of his scientific investigations as well as all the difficulties he faced in Istanbul. He confessed that he had to carry out his scientific work mainly to escape from such difficulties that were also experienced by his predecessors [12].

A Turkish physiologist, Colonel Sakir Bey, once asked to Remlinger: “What can you do with your humble sailboat in waters where even mighty ships have sunken?” [9, 12]. As an answer, he discovered the ultra filterability of the rabies virus with Rifat Bey, and made several other very important discoveries in Istanbul.

When he passed away in 1964, he had gained a worldwide fame both in human and veterinary medicine.

Acknowledgements

We would like to thank to the employees of the Archives Department of the Institute Pasteur for original documents, Assistant Professor S. Mehmet Soylu for the meaning of some French words and Associate Professor Kadir Yesilbag for checking the sections related to virology.

References