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The early use of Pasteur's rabies vaccine in the United States

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ABSTRACT

Louis Pasteur's vaccine against rabies was introduced in France during 1885. A year later it became available within the United States. This article tells the story of the first use of the Pasteur vaccine in America and describes the early history of the vaccine's production and distribution across the country by Pasteur Institutes established for this purpose. Highlights of Pasteur's landmark studies on rabies are presented: research which pioneered the field of virology and the use of immunization to prevent infectious diseases.

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1. Introduction

Starting in 1885, persons bitten by rabid animals travelled from all over the world to Paris, France to receive Louis Pasteur's newly developed vaccine against rabies. Four American boys from Newark, New Jersey, bitten by a stray dog, were sent to Paris during December 1885 for the Pasteur vaccination and returned home in January 1886 amidst much publicity throughout the country [1]. Thanks to the efforts of one surgeon, Dr. Valentine Mott, the Pasteur vaccine soon became available for clinical use in the United States for the first time.

On July 5, 1886, a seven year old boy named Harold Newton Newell, became the first person to receive the Pasteur vaccine in America. This is the story of that historic event and an account of the development of the vaccine and its early use within the United States.

2. The patient: Harold Newton Newell

On June 24, 1886, Harold Newell from New Jersey, was bitten in his right axilla and shoulder by the family's pet dog, suspected to

be rabid [2,3]. The dog was "proved" to be rabid by inoculation studies on two rabbits. One rabbit, inoculated presumably with the dog's infected brain tissue, died, and the second rabbit showed "violent signs of rabies" [2].

Eleven days later, on July 5, 1886, Harold Newell received the first of a planned series of ten inoculations of the Pasteur rabies vaccine. In the Pasteur vaccination protocol, each inoculation was administered by a hypodermic syringe, subcutaneously, in the upper abdomen. The vaccination process was supervised by Dr. Valentine Mott, a New York surgeon. Harold Newell was vaccinated in the American Pasteur Institute's space in the Carnegie laboratory in New York City [1]. His father, Dr. William H. Newell, a physician who lived in Jersey City Heights, New Jersey, signed the consent forms permitting the treatment. The story of Harold Newell's vaccination was subsequently widely reported in newspapers across the United States [2–4].

Newell received only 4 of the 10 planned inoculations of the rabies vaccine due to a series of accidents that befell him, forcing an early end to the vaccination process [5]. The accidents began when Newell was hit by a thrown stone and badly cut. He also fell down elevated railroad stairs injuring his nose with severe epistaxis. Finally, Newell cut his wrist and a branch of his ulnar artery on a broken pitcher, resulting in a severe hemorrhage [5].

The last mention of Harold Newell's condition was in a report by Valentine Mott read before The American Social Science Association of Saratoga on September 8, 1886 [5]. The report indicated that the boy was stable, without any rabies symptoms, two and a

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half months after the dog bite. There are no further reports on the fate of Harold Newell.

3. The physician: Dr. Valentine Mott

Dr. Valentine Mott (1852–1918) began his career as a surgeon in 1879, when he joined Bellevue hospital as an attending physician, following in the footsteps of his father and grandfather, who were distinguished surgeons. Mott championed the Pasteur vaccine technique in the United States and in 1886 he helped to incorporate the first Pasteur Institute in America, the American Pasteur Institute, located in New York City, for this purpose.

Mott sailed to Paris in March 1886 to study how the Pasteur rabies vaccine was prepared and administered, arriving there on April 6th. He spent a month in Pasteur's laboratory, describing his experiences as follows:

During the month of April last I visited Pasteur's laboratory as the representative of the American Pasteur Institute. I was kindly received by him and his assistants, and everything in the process of his method of inoculation shown to me, from the primary trepanation and introduction of the virus under the dura mater of a well rabbit to the inoculation of the human being with the spinal cord of a rabbit which had died of rabies [5].

Upon leaving Paris, Mott received from Pasteur's laboratory a rabbit inoculated that day with rabies virus. Nine days later the rabbit died, having developed signs of paralysis two days before. Arriving in the United States the next day, Mott dissected out its spinal cord and began to propagate the rabies virus through subdural inoculation of the infected spinal cord into healthy rabbits. Those rabbits subsequently developed rabies, providing Mott with the necessary infected spinal cords to produce, by desiccation, the Pasteur rabies vaccine that was prepared and used to vaccinate Harold Newell and others.

In his 1886 presentation, Valentine Mott reported that he vaccinated 3 additional patients with the complete series of rabies inoculations and all were doing well [5]. In total, the American Pasteur Institute vaccinated about a dozen persons against rabies during 1886 but was forced to close in 1887 due to lack of public and financial support [1,6]. Other Pasteur Institutes, however, soon opened in the United States: in New York City and Chicago during 1890, in Baltimore during 1897, and in Atlanta, Pittsburgh and St. Louis in 1900 [1]. About twenty-five more institutes were opened after 1900 [1]. Of the all the institutes, perhaps the most famous was the New York Pasteur Institute. Many other Pasteur Institutes were also opened in other countries throughout the world.

4. The New York Pasteur Institute 1890–1918

During the late Nineteenth Century human rabies cases were widespread within the United States but limited in numbers. A statistic from health officers of 73 American cities indicates that there were 230 rabies deaths between 1890 and 1900 [7]. In New York City, there were 39 rabies deaths from 1870 thru 1884 [1]. Although rabies was infrequent, the disease was greatly feared by the public since it was invariably fatal. It was against this historical backdrop that the New York Pasteur Institute opened in 1890 under the direction of Dr. Paul Gibier (1851–1900).

The New York Pasteur Institute was not connected with the American Pasteur Institute which had closed in 1887. They were different enterprises with different locations and staff. Both the American Pasteur Institute and the New York Pasteur Institute were established to provide rabies vaccination within the United States and thus spare patients the costly expense and treatment delays involved in travelling to France in order to get vaccinated.

What enabled the New York Pasteur Institute to succeed, where the American Pasteur Institute had failed, were the following: (1) the New York Pasteur Institute had better financial backing, (2) it had a broader entrepreneurial scope that made it into a major pharmaceutical supplier of vaccines and ant-toxins, (3) by 1890 there was a greater acceptance among the American medical community of the Pasteur rabies vaccine as being effective in preventing the disease, (4) it was led by Paul Gibier, a French physician who was uniquely qualified for this position with a strong background in rabies and also excellent administrative skills.

Gibier had a strong background in microbiology, having completed his doctoral thesis on rabies while at the University of Paris [6]. He was also experienced in the use of laboratory methods for medical research and thus was able to pioneer a private research laboratory at the New York Pasteur Institute. Gibier was also an able administrator, securing funding for the New York Pasteur Institute from public and private sources as well as from the New York State government [6].

In 1893, Gibier began to publish a quarterly medical journal, the *New York Therapeutic Review*, later called *Bulletin of the New York Pasteur Institute*, which updated readers on the latest developments in rabies research and the latest advances in the treatment of infectious diseases. During the 1890s, Gibier expanded the scope of the New York Pasteur Institute to include the production of the newly developed diphtheria and tetanus anti-toxins [6].

Gibier also expanded the facilities of the New York Pasteur Institute which included an office on Twenty-third Street in Manhattan and, in 1893, the construction of a five story building on Central Park West. In 1895, Gibier purchased 200 acres in Suffern, New York, to set-up barns for large animals, such as horses and cows, that would provide diphtheria anti-toxin and other biological treatments. The facility also included a sanitarium for patients. The fee for a course of rabies vaccine was \$100, exclusive of room and board, but many patients were treated for free [6].

A major blow to the New York Pasteur Institute came in 1900 when Paul Gibier was killed in a carriage accident. His nephew took over the operations of the New York Pasteur Institute, limiting its scope to rabies vaccination, and he sold the Suffern facility. Another threat to the New York Pasteur Institute was increasing competition from the New York City Department of Health, which also provided rabies vaccination. The development of prepared injections and longer shelf life for the rabies vaccine made it possible for the health department to distribute the vaccine to private physicians and hospitals for widespread administration across the state. The New York Pasteur Institute remained open until 1918, having vaccinated 1307 persons between 1890 and 1899, with 9 rabies deaths (0.68% mortality) and 3198 persons between 1900 and 1916, with 5 rabies deaths (0.16% mortality) [8].

5. The Pasteur vaccine against rabies

5.1. Background

Louis Pasteur (1822–1895) was an outstanding scientist. Among his first, and arguably his best work, was the observation of isomerization of crystals. But his career was one that encompassed many diverse studies and discoveries. Pasteur studied the cause of spoilage of beer, wine and milk and demonstrated this was linked to contamination of these liquids with “germs.” He demonstrated that catastrophic disease in silk worms in the south of France was due to contamination with living germs. He provided the definitive proof that the theory of spontaneous generation was false and that the “germ theory” was correct, which formed the basis of modern microbiology. He turned his interest to prevention, and before

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