Horses as Heroes in the Fight Against Diphtheria

At the turn of the 20th century, diphtheria (Greek for "pair of leather scrolls") was one of the leading and most feared killers of children ages 2 through 14. In the severe laryngeal form of this contagious upper respiratory disease, a thick membrane sheath forms at the back of the throat, obstructing airways and potentially leading to heart, kidney, and neurologic damage. Today, thanks to widespread DPT vaccination, this highly contagious disease has been largely eradicated in industrialized countries except for sporadic outbreaks. But it is little known that horses had a significant early role in this medical triumph.

The causative organism, *Corynebacterium diphtheriae*, was first recognized by Theodor Albrecht Edwin Klebs in 1883 and then successfully cultured and associated with the disease by Friedrich Loeffler in 1884. In 1890, German microbiologist Emil von Behring discovered the diphtheria toxin and developed an antitoxin that did not kill this anaerobic bacterium, but rather neutralized the poisons released into the body. Having also discovered that animal blood contained antitoxins, von Behring collected blood, removed the clotting agents, and injected the serum into human patients. When the first successful human patient was "cured" of diphtheria in Berlin in December 1891, this news rocked the medical community and resulted in intense activity on antitoxin production in Germany and France. Von Behring would later earn the first Nobel Prize in Medicine or Physiology in 1901 for this work.



Figure 1. Engraving of Hermann Michael Biggs, MD (1859-1923).

From: Winslow C-E A. *The life of Hermann M. Biggs, MD, DSc, LLD.* Philadelphia: Lea & Febiger, 1929; frontispiece. HathiTrust Digital Library, https:// hdl.handle.net/2027/ mdp.39015006647914 How do horses fit into the picture? Both Dr. von Behring in Germany and Louis Pasteur's assistant, Dr. Emile Roux, in Paris independently were using horses for large-scale production of the diphtheria antitoxin.

On our side of the Atlantic, interest in this major development was also considerable. During a scientific tour of Europe in the summer of 1894, Dr. Hermann M. Biggs (1859-1923), (Fig. 1) the chief bacteriologist of the New York City Health Department, was so excited about the stunning results of diphtheria serotherapy that he immediately wired home to acquire some horses. Without appropriated funding in the City's budget that year, Dr. Biggs and a colleague paid for the 13 horses themselves.

The first doses of what would become a steady supply of fresh serum became available in New York City on January 1, 1895. In the first 5 years alone, the death rate decreased dramatically—by nearly 100 percent—and mortality steadily declined in the following decades. Magazines and newspapers, such as the *New York Herald*, hailed the "antitoxin horses" and helped raise funds to support the horses that were stabled for nearly two decades at the New York College of Veterinary Surgeons on East 57th Street and Third Avenue in New York City.

The six-month production process involved systematically injecting horses with small amounts of diphtheria toxin. When sufficient neutralizing antibodies, or antitoxin, had been generated, two to four pints (or up to the "standard six litres") of blood would be drawn and refrigerated, and the clotted blood removed. The resulting antitoxin serum was chemically purified and sent to hundreds of clinical administration stations around the city's boroughs. While antibody production was tried in some sheep, goats, and dogs, "horses prevailed because they were larger and better antitoxin factories." Dr. Harry D. Gill, a veterinary professor, described the production process in detail at the March 5, 1895 meeting of the Veterinary Medical Association of New York County. He indicated that of the 75 horses under his care, "three-fourths are either balkers, kickers, runaways, or have some bad habit which renders them unfit for general use" as streetcar, wagon, or carriage horses.

In a public relations campaign, Dr. Biggs "took great pains to explain how the horses were treated like hospital patients, how the healthiest horses were selected for this vital task, and that the animals were fed wholesome food and lived in pristine stables." (Markel) "Most survived the injections with nothing more than a fever and loss of appetite, but over the years quite a few horses succumbed to even tiny doses of toxin." (Markel)

A "magnificent, large animal" had been "condemned" as being "useless" after serving for many years with the Street Cleaning Department. Dr. Aaron Silkman, veterinarian in charge of the laboratory, pleaded against killing the horse and took him into the serum program. This remarkable old horse, known only as "Horse 397," is credited with donating more than 1,000 quarts of blood during 16 months in the program.

In 1906, 59 antitoxin horses had been moved upstate to the city's Otisville farm and tuberculosis sanitarium. The City Health Department "continued to mass-produce antitoxin until well after World War II" and sold it worldwide until municipal health departments began phasing out production. When the Otisville facility was sold to a biotech company in 1987, it was stipulated that the "retired horses living there would be cared for until they died."



Figure 2. In a second serum operation in New York State, blood is shown being drawn from a horse to obtain diphtheria antitoxin at the Antitoxin Laboratory of the New York State Department of Health located first on Yates Street in downtown Albany and then moved to the present Wadsworth Center in nearby Guilderland, New York. Photo courtesy Wadsworth Center, New York State Department of Health http://www.wadsworth.org/ docs/poster_3.shtml

The New York State Department of Health had also established an Antitoxin Laboratory in 1901 to standardize and manufacture diphtheria antitoxin. (Fig. 2) It was located first in a two-story building on Yates Street in a residential area of downtown Albany and then moved to the present Wadsworth Center in nearby Guilderland, New York. Dr. Biggs became state health commissioner in 1914.

The application of antitoxin represents one of the first science-based remedies for infectious diseases. According to Simon (p. 181), "the use of blood serum from immunized animals to treat diseases of humans—serotherapy—marks an important development in the history of science and the history of pharmacy at the end of the nineteenth century." (Fig. 3) Diphtheria is largely forgotten as a major threat these days, but we should remember the important role played by these early equine heroes and the veterinarians who cared for them.



Figure 3. Administering diphtheria antitoxin derived from horse serum, 1895. Source: The Historical Medical Library of The College of Physicians of Philadelphia. Biggs, HM, and Parke, WH. *Diphtheria antitoxin*. Detroit: Park, Davis and Company, 1895. Creator: The Historical Medical Library of The College of Physicians of Philadelphia http://www.historyofvaccines.org/content/antitoxin-treatment

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