The Public Health Service and the Control of Biologics

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In December 1901, the first Nobel Prizes were awarded, and the recipient of the initial prize in Medicine and Physiology was the German physician and scientist Emil von Behring. The award recognized "his work on serum therapy, especially its application against diphtheria."

In the early 1890s, von Behring and his colleagues had created a scientific sensation with the introduction of an antitoxin that neutralized the toxin produced by the causative organism of diphtheria. The antitoxin was produced by injecting animals with the diphtheria toxin, producing antitoxins in their blood serum. This serum could then be used to treat diphtheria victims. The involvement of the Public Health Service with biologics such as the diphtheria antitoxin began soon after this important therapeutic breakthrough was made.

Clinical studies of the antitoxin published by Emile Roux in 1894 showed that the mortality due to diphtheria in Paris hospitals was reduced from 52 to 25 percent with antitoxin therapy. By early 1895, the diphtheria antitoxin was being produced in the United States by the New York City Board of Health and by the Hygienic Laboratory of the Marine Hospital Service (the forerunner of the Public Health Service). Soon thereafter, commercial firms such as Parke Davis and Company and Mulford Laboratories were manufacturing the antitoxin on a large scale. The horse was the animal of choice for large-scale production of the antitoxin.

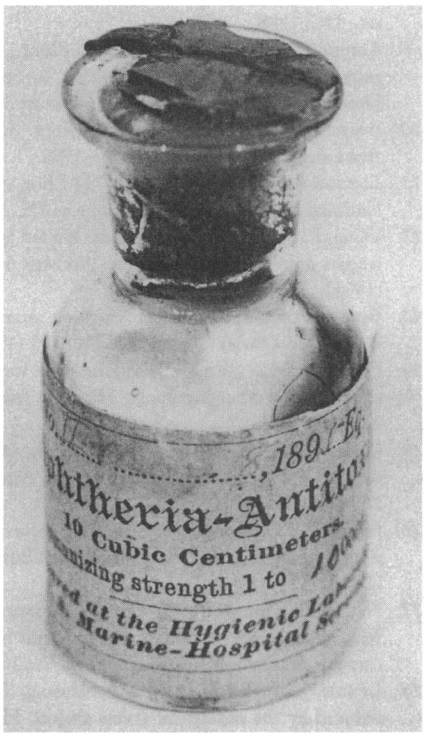
Shortly after the introduction of serum therapy for diphtheria and tetanus, concerns began to be expressed about the need to regulate such products. Standards of potency and purity were needed to insure the safety and efficacy of these drugs, which could vary greatly in strength and could easily become contaminated if their production was not carefully controlled. There was no government regulation of these products in the United States, however, until a tragedy forcefully brought the issue to public attention.

In the fall of 1901, 13 children died in St. Louis after receiving diphtheria antitoxin. An investigation revealed that the antitoxin had been accidentally contaminated with tetanus bacillus when the St. Louis Board of Health produced it from a horse that had contracted tetanus. This was not the first instance of fatalities caused by the administration of antitoxin, but the number of deaths, all of them children, led to widespread publicity. Pressure mounted for legislation to regulate the manufacture of diphtheria antitoxin and related products.

With the cooperation of the Hygienic Laboratory, the Medical Society of the District of Columbia proposed a law regulating the sale of biologics such as vaccines and antitoxins. The bill was quickly enacted and signed into law by President Theodore Roosevelt on July 1, 1902. The act established a board consisting of the Surgeons General of the Army, the Navy, and the Marine Hospital Service and gave the board the authority (with the concurrence of the Treasury Department) to issue regulations for licensing manufacturers of biologics.

The Public Health and Marine Hospital Service (a law passed on the same day as the biologics act changed the name of the Service) was granted the authority to inspect the premises of manufacturers of these products.

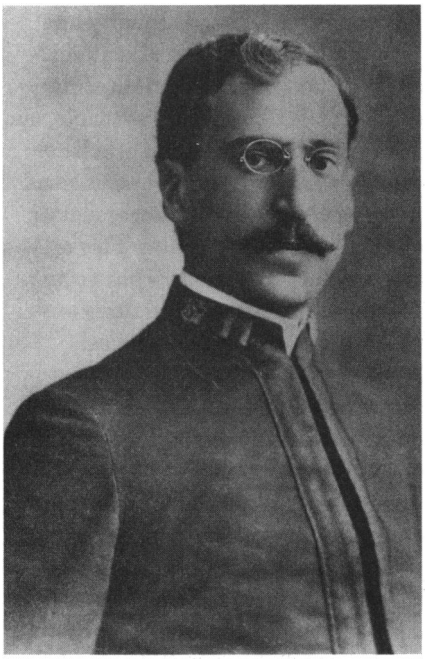
The Hygienic Laboratory of the Public Health and Marine Hospital



A bottle of diphtheria antitoxin produced by the Hygienic Laboratory in 1895. (Courtesy of the Smithsonian Institution.)

Service was assigned the responsibility for the administration of the act, leading to an increase in the size and scope of the institution. The Laboratory issued licenses, inspected manufacturing facilities, and regularly tested the products for purity and potency. It also established the standards of potency for biologics. The 1902 act helped to stimulate increased research activities at the Hygienic Laboratory, foreshadowing its evolution in 1930 into the National Institute (later Institutes) of Health (NIH).

The scope of activity of the Hygienic Laboratory in the regulation of drugs increased in 1917, when the United States entered World War I. Before the war, this country had depended upon Germany for its supply of salvarsan and neosalvarsan, arsenical drugs used in the treatment of syphilis. In Germany, because of the difficulties in obtaining uniform preparations of



Milton J. Rosenau was director of the Hygienic Laboratory at the time when it assumed responsibility for the control of biologics.

these drugs, each batch produced by the manufacturer was tested in the laboratory. With the entry of the United States into the war, the supply of German drugs was cut off. The Federal Trade Commission abrogated German patent rights and licensed American manufacturers to produce the arsenical drugs. It seemed a logical step to bring the testing and control of arsenicals under the same system as biologics, and so the Hygienic Laboratory was given this responsibility.

Yet there was by this time another Federal agency involved with the regulation of therapeutic drugs, the Bureau of Chemistry of the United States Department of Agriculture. The 1906 Food and Drug Act had assigned the responsibility of administering its provisions to the Bureau, the regulatory arm of which evolved into the Food and Drug Administration (FDA). The authority of FDA expanded, especially as a result of the 1938 Food, Drug, and Cosmetic Act, but the responsibility for biologics control remained with NIH for many years. It was not until 1972 that the regulation of biologics was transferred to FDA, which by this time was also an agency of the Public Health Service.

The triumphs of diphtheria antitoxin at the beginning of the era of biologics had been marred by the St. Louis incident that led to the passage of the 1902 Biologics Act. Even the precautions taken under that law, however, were not sufficient to prevent another tragedy, associated with the introduction of another great medical advance. In 1955, the results of clinical trials with the polio vaccine developed by Dr. Jonas Salk were announced. The vaccine was a spectacular success, and appeared to be safe as well as effective. The Public Health Service (PHS) immediately licensed several manufacturers to produce the vaccine, and a national immunization campaign was launched. Soon thereafter, however, reports began to come in of cases of poliomyelitis among those who had received the vaccine.

Testing vaccines and serums for purity and potency at the National Institute (later Institutes) of Health, about 1930.

Investigations by epidemiologists at the Communicable Disease Center (later the Centers for Disease Control and Prevention) of the PHS quickly established that the cases of polio were among those who had received lots of the vaccine produced by one company, Cutter Laboratories. Live viruses were found in some of the Cutter vaccines and the company's lots were recalled. The vaccination campaign was temporarily halted, but it was resumed within a week when it was shown that the vaccines from other manufacturers were safe.

Unfortunately, 71 cases of paralytic polio and 11 deaths had occurred as a result of the Cutter incident. In the long run, of course, the Salk vaccine turned out to be a milestone in preventive medicine and led to a reduction of the incidence of polio in the United States of 87 percent in the first few years after its introduction.

The role of the Public Health Service in the development, distribution, and control of biologics began a century ago. Over time, that role has expanded to involve several PHS agencies, helping to insure the nation a safe and effective supply of vaccines and related products.

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