Pioneers in Vaccinology

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Edward Jenner

Edward Jenner is often called “the father of immunology”, and his work is said to have “saved more lives than the work of any other human”. Edward Jenner (1749 – 1823) was an English physician and scientist who was the pioneer of smallpox vaccine, the world’s first vaccine.

He noted that milkmaids were generally immune to smallpox and so postulated that the pus in the cowpox blisters protected them from smallpox.

On 14 May 1796, Jenner inoculated James Phipps, an eight-year-old boy with pus from cowpox blisters on the hands of Sarah Nelmes. She was a milkmaid who had caught cowpox from a cow called Blossom, whose hide now hangs on the wall of the St George’s medical school library. The boy was later challenged with variolous material and showed no sign of infection.

Donald Hopkins has written, Jenner’s unique contribution was not that he inoculated a few persons with cowpox, but that he then proved [by subsequent challenges] that they were immune to smallpox. Moreover, he demonstrated that the protective cowpox pus could be effectively inoculated from person to person, not just directly from cattle.” Jenner wrote in the context of administration of smallpox vaccine to thousands across the globe, “I don’t imagine the annals of history furnish an example of philanthropy so noble, so extensive as this.”

In 1979, the World Health Organization declared smallpox as an eradicated disease. Jenner’s vaccine also laid the foundation for contemporary discoveries in immunology.

In 2002, Jenner was named in the BBC’s list of the 100 Greatest Britons following a UK-wide vote. The lunar crater Jenner is named in his honor.

Louis Pasteur

Louis Pasteur is renowned for his discoveries of the principles of vaccination, microbial fermentation and pasteurization; Louis Pasteur (1822 – 1895) was a French chemist and microbiologist. He created the first vaccines for rabies and anthrax.

Pasteur’s later work on diseases included work on chicken cholera. During this work, a culture of the responsible bacteria had spoiled and failed to induce the disease in some chickens he was trying to infect.

His assistant, Charles Chamberland, had been instructed to inoculate the chickens after Pasteur went on a holiday. Chamberland failed to do this, but instead went on holiday himself. On his return, the month-old cultures made the chickens unwell, but instead of the infections being fatal, as they usually were, the chickens recovered completely. Chamberland assumed an error had been made, and wanted to discard the apparently faulty culture when Pasteur stopped him.

Pasteur guessed that the recovered animals now might be immune to the disease. In the 1870s, he applied this immunization method to anthrax, which affected cattle.

The difference between smallpox vaccination and anthrax or chicken cholera vaccination was that the weakened form of the latter two disease organisms had been “generated artificially”. Therefore a naturally weak form of the disease organism did not need to be found as in the case of smallpox. This discovery revolutionized work in infectious diseases, and

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Pasteur gave these artificially weakened diseases the generic name of “vaccines”, in honor of Jenner’s discovery.

Pasteur produced the first vaccine for rabies by growing the virus in rabbits, and then weakening it by drying the affected nerve tissue. In *The Story of San Michele*, Axel Munthe writes of the rabies vaccine research: “Pasteur himself was absolutely fearless. Anxious to secure a sample of saliva straight from the jaws of a rabid dog, I once saw him with the glass tube held between his lips draw a few drops of the deadly saliva from the mouth of a rabid bull-dog, held on the table by two assistants, their hands protected by leather gloves.”

**Jonas Salk**

*Jonas Edward Salk* (1914 – 1995) was an American medical researcher and virologist. He discovered and developed the first successful inactivated polio vaccine. Until 1957, when the Salk vaccine was introduced, polio was considered one of the most frightening public health problems in the world. Scientists were in a frantic race to find a way to prevent or cure the disease. In 1948, Salk undertook a project funded by the National Foundation for Infantile Paralysis to determine the number of different types of polio virus. Salk saw an opportunity to extend this project towards developing a vaccine against polio, and, together with the skilled research team he assembled, devoted himself to this work for the next seven years. The field trial set up to test the Salk vaccine was, according to O’Neill, “the most elaborate program of its kind in history, involving 20,000 physicians and public health officers, 64,000 school personnel, and 220,000 volunteers.” Over 1,800,000 school children took part in the trial. When news of the vaccine’s success was made public on April 12, 1955, Salk was hailed as a “miracle worker” and the day almost became a national holiday. In 1960, he founded the Salk Institute for Biological Studies in La Jolla, California, which is today a center for medical and scientific research.

**Albert Sabin**

*Albert Bruce Sabin* (1906 – 1993) was an American medical researcher best known for having developed an oral polio vaccine. The Sabin vaccine is an oral vaccine containing weakened forms of strains of polio viruses. Sabin first tested his live attenuated oral vaccine at the Chillicothe Ohio Reformatory in late 1954. From 1956-1960, he worked with Russian colleagues to perfect the oral vaccine and prove its extraordinary effectiveness and safety. The Sabin vaccine worked in the intestines to block the poliovirus from entering the bloodstream. Thus, the oral vaccine broke the chain of transmission of the virus and allowed for the possibility that polio might one day be eradicated.

Between 1955 and 1961, the oral vaccine was tested on at least 100 million people in the USSR, parts of Eastern Europe, Singapore, Mexico, and the Netherlands. The first industrial production and mass use of oral poliovirus vaccine (OPV) from Sabin strains was organized by Soviet scientist Mikhail Chumakov. This provided the critical impetus for allowing large-scale clinical trials of OPV in the United States in April 1960 on 180,000 Cincinnati school children. The mass immunization techniques that Sabin pioneered with his associates effectively eradicated polio in Cincinnati. Against considerable opposition from the March of Dimes Foundation, which supported the killed vaccine, Sabin tried to license his live oral attenuated vaccine. While the Public Health Service stalled, the USSR sent millions of doses of the oral vaccine to places with polio epidemics, such as Japan, and reaped the humanitarian benefit.

**Albert Calmette and Camille Guerin**

*Léon Charles Albert Calmette* (1863 –1933) was a French physician, bacteriologist and immunologist, and an important officer of the Pasteur Institute. He
discovered the Bacillus Calmette-Guérin, an attenuated form of *Mycobacterium* used in the BCG vaccine against tuberculosis. Calmette’s main scientific work was to develop a vaccine against tuberculosis, which, even at that time, was a giant killer disease. Using Pasteur’s approach, Calmette investigated how immunity would develop in response to attenuated bovine bacilli injected in animals. This preparation received the name of its two discoverers (*Bacillus Calmette-Guérin*, or BCG, for short). Attenuation was achieved by cultivating them in a bile-containing substrate. From 1908 to 1921, Guérin and Calmette strived to produce less and less virulent strains of the bacillus, by transferring them to successive cultures. Finally, in 1921, they used BCG to successfully vaccinate newborn infants in the Charité in Paris.

**Jean-Marie Camille Guérin**

Jean-Marie Camille Guérin (1872–1961) was a French veterinarian, bacteriologist and immunologist who, together with Albert Calmette, developed the Bacillus Calmette-Guérin (BCG), a vaccine for immunization against tuberculosis. Camille Guérin was born in Poitiers to a family of modest means. His father died of tuberculosis in 1882 (as well as his wife, in 1918). In 1897, he joined the Institute Pasteur de Lille (Lille, France) and started to work with its director, French physician, bacteriologist and immunologist Albert Calmette (1863–1933). He discovered in 1905 that the bovine tuberculosis bacillum, the *Mycobacterium bovis*, could immunize the animals without causing the disease. He and Calmette developed ways to attenuate the pathogenic activity of Mycobacterium, using successive transferrals of culture. In 1908, after successfully obtaining an immunologically active preparation that could be used to produce a vaccine, he published with Calmette the results of what was named the BCG. In 1919 he was promoted again, this time to Head of Services. Finally, in 1921, after 230 passages of the BCG culture, they obtained an effective vaccine that could be used in humans. In 1928 he moved to Paris to become the director of the Tuberculosis Service at the Pasteur Institute.

**References**