Past and future of vaccination and immunology - Part 1: The origin of vaccination and the science of immunology

Edward Jenner is the father of vaccination and Lois Pasteur of immunology. The background and story about their achievements are explained.

Although evolution provided us with the means to fight microorganisms, we still succumb to deadly germs. In history, not only plaque but also smallpox was one of the most terrible diseases. Smallpox might have evolved when mankind changed from being hunters and gatherers into farmers living in more crowded and defined settlements during the agricultural revolution some 10.000 years ago.

Some highlights of the history of smallpox from ancient times to the 20th century

Smallpox was known to the Egyptians and ancient Asian cultures, such as China and India. The disease spread to the West following the Arabic expansion and the Crusades. Smallpox influenced history. The Aztecs and the Incas in South America, for example, were defeated by only a small number of Spanish and Portuguese conquistadores. In Europe, smallpox was a severe public health problem as well. During the 18th century, about 400.000 people died on smallpox each year, and those who survived, one-third, turned to be blind (1, 2).

The name 'smallpox' originates from England in the 15th century. At that time, the name distinguished smallpox from syphilis, which was recognized as the great pockes. In former times, the word 'variola' was commonly in use since around 570 AD. That 'variola' don't attack those who already once suffered from the disease was known since about 430 BC (3). So, it was a natural step to expose healthy persons with material from those suffering from the disease, expecting that the healthy will remain healthy and not acquire variola. The method was called either 'inoculation' or 'variolation'. A lancet was used to apply subcutaneously material derived from a ripe pustule from a diseased individual on the arms or legs of the non-diseased one. Variolation was practiced in many parts of the world and brought into Europe at the beginning of the 18th century. The procedure was not without risk. About 2% to 3% variolated persons got the disease anyhow and died from it or fell ill because of other infectious diseases, such as tuberculosis and syphilis. The germs for both diseases were occasionally and accidentally transmitted through the inoculated material.

Variolation introduced to England

To England, variolation was brought in 1721 by the wife of a diplomat, Lady Mary Wortley Montague (2). She learned about the practice at the Sublime Porte of the Ottoman Empire. Once she suffered from smallpox, what might explain her interest in variolation. Following her initiative, the embassy surgeon, Charles Maitland, inoculated her young son. After returning to London, belonging to the English aristocrats, she accomplished to have Charles Maitland variolating her four-year-old daughter in the presence of physicians of the royal court. The event became known to the royal family, and Maitland got the royal license for several trials, which all went well. The Princes of Wales then permitted Maitland to inoculate two of her daughters.

The Princess of Wales, Caroline of Ansbach, is a remarkable historical figure. The later Queen Caroline, married to King Gorge II of England, suffered from smallpox once herself.

She was highly respected and had considerable influence on politics. Her authority might have helped that variolation was generally accepted in England after 1722.

Who vaccinated against smallpox first?

Another historical figure benefited from the developments in England. An eight-year-old boy was inoculated against smallpox in 1757 (1, 4). His name, Edward Jenner. Edward was very interested in science and nature. Because of his academic achievements, he was already a member of the prestigious Royal Society of London while working on smallpox vaccination in his fortieths (2, 5). In history, he is known as the one who turned variolation into vaccination.

To country doctors in England was known that infected with cowpox might prevent smallpox. The idea to inoculate cowpox to avoid variola wasn't far-fetched. So the very first in 'vaccinating' might have been Benjamin Jesty in 1774, who transmitted cowpox from the udders of cattle to the arm of his wife and two boys (6). Jesty may have been the first 'vaccinating' humans. However, Edward Jenner is given credit for the breakthrough in the fight against smallpox at the end of the 18th century.

The historical moment and the aftereffect

The historical event included Sarah Nelms, a young dairymaid, who acquired cowpox and had pustules on her hand and arm. From her stuff was taken, and an 8year old boy, James Phipps, was inoculated by Jenner on the 14th of May 1796. July 1796, Jenner inoculated matter from a fresh smallpox lesion on Phipps again. Phipps got some fever and pain in the axillae but otherwise was spared from human smallpox (7).

Jenner couldn't publish his experiment but continued to work on the topic and added more cases to the trial. Privately he published a small booklet with the title 'An injury into the Causes and Effects of the Variolae Vaccinae, a disease discovered in some of the western counties of England, particularly Gloucestershire and Known by the Name of Cow Pox'. Jenner not only introduced the term 'vaccination', taken from the Latin word 'vacca' cow but supported the method with a sound scientific background (5). The more pragmatic view of other medical practitioners didn't push them into scientific inquiries. Jenner was 'not only a bright English country doctor' but had the vision of eradicating the 'dreadful' smallpox disease from the world. A WHO team accomplished this in 1977 when the last naturally occurring case of smallpox was registered in Somalia.

Louis Pasteur and his accomplishments

Jenner might be regarded as the father of immunology and vaccination, but then, Louis Pasteur should be the second one, living almost a century after Jenner (8). Jenner vaccinated the boy James Phipps in 1796, and Louis Pasteur was behind vaccinating against rabies in 1885 (9). Jenner stimulated an immune response against smallpox, with material from a virus, causing a similar disease in animals but non-pathogenic for humans. Pasteur saved the life of Joseph Meister with repeated daily injections of the inactivated form of the Rabies lyssavirus.

Pasteur is not just only a historical figure to be remembered for his contribution to vaccine developments. He graduated in mathematics, physics, and chemistry and became a professor at the University of Strasbourg. While exploring the course of fermentation, he recognized

the role of yeast and microorganisms in the process. Pasteurization goes back to his method to slightly expose freshly bottled wine to the heat of 50^0 to 60^0 C to keep its quality. Today, without pasteurization, milk would still be one of the most dangerous items consumed. Row milk is easily contaminated with pathogens and would be very dangerous, especially in the absents of the colling chain. Working to prevent infectious diseases, he saved the silk industry by sorting out worm eggs from infected female worms and saved farmers from losing chicken through fowl cholera and cattle and sheep from anthrax (10). He also worked with dogs to prevent them from contracting rabies.

Pasteur, dogs, and rabies

Rabies is a deadly viral disease. Once symptoms occur, the illness cannot be treated, and death is inevitable. It is estimated that still, 56.000 people die worldwide. The disease affects the nervous system and is transmitted by several animals. The most common reason for transmission is dog bites.

Pasteur started with experiments already proofed to be successful with dogs. He took virulent virus material from the spinal cords of rabid street dogs and inoculated them into rabbits. By opening the rabbit's skull, the material was inoculated under the dura mater of the brain. The procedure was repeated from rabbit to rabbit for about 20 times or more to ensure that he could gain a consistently virulent virus. Bits of spinal cords from the rabbit he dried in the air within a container with some potassium at the bottom. This gradually decreased the virulence until it was gone. That non-infectious material then was inoculated into about 50 dogs, which did not develop the disease (9).

Successful fight against certain death

Pasteur was not a medical doctor while Jenner was. For the ‘emergency’ treatment of Joseph Meister, Pasteur was talked into it by Dr. Vulpian and Dr. Grancher from the Faculty of Medicine of the University of Paris (9). Some months later, a shepherd boy, Jean-Baptiste Jupille, was vaccinated as well. From this time onwards, hundreds of other victims of dog bites were vaccinated (10), and the method was adopted throughout the world.

Meister got vaccinated 13 times throughout 15 days. It was realized later, from day seven onwards, that the boy got vaccines being virulent. Virulence was assessed by testing the inoculated material in rabbits. Up to day seven, rabbits did not fall ill. From the eighth day onwards, the material vaccinated was virulent for the rabbits but not for the patient any longer. Of course, at the time of Pasteur, an infective agent, as it is now known as a virus, could neither be seen nor tested in the way as it is done today.

Conclusion

Pasteur concluded, from his experience with ‘attenuated’ vaccines, that diseases could be prevented, but the other way round, that the agent causing the disease could be infectious to man and animals (10). His argumentation helped oppose the miasma theory, which was finally proved wrong by Robert Koch and others. As far as immunology is concerned, others might have been ingenious in microbiology as well, but there is then saying that ‘Jenner discovered vaccination, but Pasteur invented vaccines’ (10).

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