# HISTORICAL NOTE

## Louis Pasteur and Rabies: a brief note

The almost universal fatality in victims of untreated human rabies surrounds the disease with understandable terror. The word comes from the Latin *rabere* to rage or rave. It was known as canine madness, or hydrophobia that produces paralysis or a vicious excitability and in man fatal encephalitis with throat spasms on swallowing.

A variety of meningoencephalitis rabies presents as a "hydrophobic" or "spastic" form and a "tranquil" or "paralytic" (rabies without hydrophobia) form, the latter with an ascending paralysis of Landry type, terminating in bulbar, respiratory, and encephalitic symptoms. The history of dog bite is often unclear if it has occurred some months earlier. Symptoms usually develop, however, 10 to 50 days after exposure; death ensues within about 10 days. In Great Britain rigid quarantine laws on the importation of all livestock led to its virtual eradication.

In 1804, Georg Gottfried Zinke first transmitted rabies[1] from a rabid dog to a normal one, and from dog to a rabbit and a hen, by injection of saliva. This proved that the disease was infectious. By 1826, Franz Christian Karl Krugelstein (1779–1864) wrote a full account of rabies, with a bibliography of 300 items.[2]

But the species susceptibility was unclear until Victor Galtier demonstrated the transmission from dog to rabbit to rabbit, in series.[3] He then immunised sheep by inoculating rabid saliva intravenously. This did not produce the disease but interestingly, protected the animals from the effects of a further inoculation.[4]

His work aroused the interest of Louis Pasteur who with C Chamberland, PPE Roux, and T Thuillier wrote the first of their papers in 1881,[5] heralding the beginning of Pasteur's studies on rabies. In further work,[6] they showed indications of the rabies virus in the blood.

> "It first lodges and multiplies in the spinal cord and brain".

He reported: When passed from dog to monkey and then from monkey to monkey, the virulence diminishes with each transmission, and then if inoculated back into dogs, rabbits, or guinea pigs, it remains attenuated. However, virulence was serially increased when passed from rabbit to rabbit, or from guinea pig to guinea pig. He was thus able to produce the virus in various degrees of virulence. Sections of rabid spinal cord from a highly virulent strain after serial passage through many rabbits were suspended in dry air; the virulence gradually diminished with time. Thus, Pasteur produced an attenuated vaccine, and successfully immunised 50 inoculated dogs.[7]

On Monday 6 July 1885, Joseph Meister, aged nine, was brought to him from Alsace having been bitten by a rabid dog on 4 July. With some reluctance, Pasteur was persuaded by Drs Vulpian and Grancher of the Académie de Médecine to give Dr Grancher the emulsion from the cord of a rabbit that had died of rabies on 21 June, and had been kept in dry air for 15 days. The child was given 13 further inoculations in 10 days with portions of the cord that were progressively fresher (more virulent), until after three months and three days he announced that the child's life was now out of danger and his health appeared excellent. On 20 October, he successfully treated another patient infected by a mad dog six days earlier. By 1886, he had treated 350 patients from all over Europe, Russia, and America.[8]

This is considered his greatest triumph. Microscopic diagnosis was later made possible by Aldechi Negri's discovery of the Negri body (1903–5). Fermi used phenol treatment of rabid tissue to prepare the Fermi vaccine in 1908. Webster and Clow first grew the virus in tissue culture in 1936, which led to human cell culture vaccine,[9] and diploid cell vaccine in 1978.

A French chemist, Louis Pasteur (1822–95), is often called the founder of microbiology.[10] In 1863, the Emperor Napoleon III instructed him to investigate diseases affecting wines. He successfully investigated *pébrine* and *flacherie*, diseases of silkworms in the 1860s and by enforcing isolation of infected silkworms controlled the illness that was destroying silk production.

His early studies on fermentation that showed that yeast acts as microorganisms that converts sugar into alcohol and not as chemical enzymes, as was believed by Liebig and others. He also claimed a specific ferment that sours milk. Just as a specific microorganism, or "germ" causes each type of fermentation, many diseases are also caused by specific ferments (*Memoire sur la fermentation appelee lactique,* 1858). Fermentation resembled the observed putrefaction of wounds. The (invisible) germs or ferments were in the air, a notion that caused disdain amongst critics of his germ theory of disease. His proof that diseases could be caused by "germs" was a novel and major discovery.[8] Pasteur showed that the virulence of infected blood was dependent on temperature and oxygen, so that fowl with their high body temperature resisted inoculation with anthrax. Following Koch's work on anthrax spores in 1876, Pasteur established that a culture grown at high temperature was less virulent and induced only a mild illness in sheep: an attenuated "anthrax vaccine". This was akin to Edward Jenner's vaccination with cowpox to immunise against smallpox.

In 1854, he became professor of chemistry and was elected as a member of the French Academy of Medicine, a singular honour. The University of Bonn conferred the MD, honoris causa in 1868, which he returned in 1871. In his own time, Pasteur achieved great celebrity culminating in a public subscription of two and a half million francs that made feasible the creation of the Pasteur Institut, in Paris. Despite a stroke at the age of 46, he continued researches undaunted until 1888. He died on 28 September 1895 at Garches, Seine-et-Oise.[8]

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### References

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