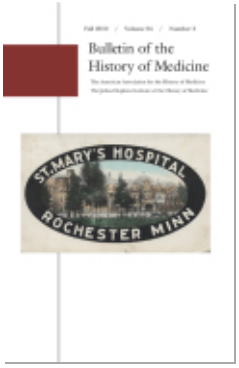
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"Living versus Dead": The Pasteurian Paradigm and Imperial Vaccine Research

PRATIK CHAKRABARTI

SUMMARY: The Semple antirabies vaccine was developed by David Semple in India in 1911. Semple introduced a peculiarly British approach within the Pasteurian tradition by using carbolized dead virus. This article studies this unique phase of vaccine research between 1910 and 1935 to show that in the debates and laboratory experiments around the potency and safety of vaccines, categories like "living" and "dead" were often used as ideological and moral denominations. These abstract and ideological debates were crucial in defining the final configuration of the Semple vaccine, the most popular antirabies vaccine used globally, and also in shaping international vaccination policies.

KEYWORDS: Semple, carbolic acid, live vaccine, Pasteur, *rage du laboratoire*, Kasauli

The development of the Semple antirabic vaccine was a pioneering but little known colonial research program. Originally developed by David Semple (an officer of the Indian Medical Service, IMS) at the Central Research Institute in Kasauli (CRI, India) in 1911, it was the most commonly used antirabies vaccine throughout the world and until 2000 the only such vaccine used in the developing countries where rabies is widespread. This article studies this unique phase of vaccine research in colonial India between 1910 and 1935. It studies the morality of using dead and live vaccines, the laboratory experiments on poor Indian patients, the determination of quantities of brain matter in vaccines, and the domestic and international public health factors, all of which defined the final configurations of the Semple vaccine. By studying the history of making a vaccine, this article captures the location of Pasteurian bacteriology within the larger ideological, political, and ethical history of bacteriology and vaccination policy in colonial India.

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The existing literature is rich in the analysis of the history of vaccine research and production through industrial and laboratory modes.[1] It has also extensively depicted the moralities of vaccine experiments (on animals and humans) and vaccination campaigns.[2] This article studies the moral debates in vaccine research with regard not to the subjects of the experiments but its *objects*, the germs used in the vaccines. The study of the debates around using "live" and "dead" vaccines also challenges some of the sociological understanding of the Pasteurian laboratory. Bruno Latour has critiqued Louis Pasteur's engagement with microbes and argued that by creating a controlled condition of existence Pasteur assumed a position of power. He posed himself stronger than the bacillus as well as the farmers, who were then subjected to his method. To challenge Pasteur's authoritative "control," Latour attributed life to the inanimate microbes.[3] However, this hylozoism does not address the essential problem of Pasteurian bacteriology.[4] As this article shows, "life" and "living" formed the core of Pasteur's engagements with microbes and were essentially constructs. Therefore, by seeking to provide life-like agency to these organisms, Latour in effect extended the Pasteurian project rather than questioning Pasteur's role in creating such divides between living and the dead microbes.

Rabies is an acute encephalitis caused by a virus that affects hot-blooded animals, including humans. It kills by attacking the central nervous system. In 1885 Pasteur identified the nervous system as the main target for its experimental reproduction and conceived means of attenuating the agent by repeated passages through rabbits. Strips of fresh spinal cord material taken from rabbits that had died from rabies were exposed to dry, sterile air for various lengths of time. This tissue was then ground up and suspended in a sterilized broth. This solution was used as a vaccine.[5]

1. Christoph Gradmann, "Locating Therapeutic Vaccines in Nineteenth-Century History," *Sci. Context* 21 (2008): 145–60; Jonathan Simon, "Monitoring the Stable at the Pasteur Institute," *Sci. Context* 21 (2008): 181–200; and J. Andrew Mendelsohn, "The Microscopist of Modern Life," *Osiris* 18 (2003): 150–70.

2. Gerald L. Geison, *The Private Science of Louis Pasteur* (Princeton, N.J.: Princeton University Press, 1995); Nicholas Rupke, ed., *Vivisection in Historical Perspective* (London: Croom Helm, 1987); and Michael E. Lynch, "Sacrifice and the Transformation of the Animal Body into a Scientific Object: Laboratory Culture and Ritual Practice in the Neurosciences," *Soc. Stud. Sci.* 18 (1988): 265–89.

3. Bruno Latour, *Pasteurisation of France* (Cambridge, Mass.: Harvard University Press, 1988), 80–86.

4. For a brilliant critique of this aspect of Latour's work, see Simon Schaffer, "The Eighteenth Century Brumaire of Bruno Latour," *Stud. Hist. Philos. Sci.* 22 (1991): 174–92.

5. "Pasteur's Method," *Pioneer Mail and Indian Weekly News*, August 12, 1896, 26–27.

Semple introduced a peculiarly British approach within this Pasteurian tradition by using carbolized dead virus, a method he adopted from his tutor Almroth Wright's work on opsonins and vaccine therapy. Historians who have worked on Pasteur and the moral and political history of bacteriology have referred to dead and living vaccines as well as their medical implications but have failed to indicate their therapeutic and ideological significance. As a consequence they have often adopted categories like "heroic" and "sterile" while discussing live and dead vaccines.[6] This not only has led to ambiguous understanding of such categories but also has given rise to misunderstanding of the side effect from antirabies vaccines often associated with live vaccines, namely "laboratory rabies," a volatile issue in Pasteur's time. This article argues that in these debates and laboratory experiments around the potency and safety of vaccines, categories like "living" and "dead" were often used as ideological and polemical categories rather than scientific ones, which acquired further political and ethical significance in colonial vaccination policies. It is this ambiguity that holds a key to the development of the Semple vaccine and its application in Asia and Africa. The debates around using living and dead vaccines refer to the two most important concerns of vaccine research, potency and safety. On one hand was the heroic potency of the living and, on the other, the sterilized safety of the dead.

Pasteur and the World of the Living

From 1854 Pasteur was concerned with the role of living organisms in causing fermentation: "[F]ermentation is an act correlated with the life and organisation of the yeast cells, not with the death or putrefaction of the cells." This led to his famous assertion, "[N]o fermentation without life."[7] Contemporary Pasteurists were fascinated by these miniscule organisms while watching their world under the microscope, the "wondrous workings

6. Gerald L. Geison, "Pasteur, Roux, and Rabies: Scientific *versus* Clinical Mentalities," *J. Hist. Med. & Allied Sci.* 45 (1990): 341–65; Kim Pelis, "Prophet for Profit in French North Africa: Charles Nicolle and the Pasteur Institute of Tunis, 1903–1936," *Bull. Hist. Med.* 51 (1997): 583–622, esp. 595–96; Ilana Löwy, "From Guinea Pigs to Man: The Development of Haffkine's Anticholera Vaccine," *J. Hist. Med. & Allied Sci.* 47 (1992): 270–309; George H. Bornside, "Waldemar Haffkine's Cholera Vaccines and the Ferran–Haffkine Priority Dispute," *J. Hist. Med. & Allied Sci.* 37 (1982): 399–422; and Derek S. Linton, "Was Typhoid Inoculation Safe and Effective during World War I? Debates within German Military Medicine," *J. Hist. Med. & Allied Sci.* 55 (2000): 101–33.

7. Keith L. Manchester, "Louis Pasteur (1822–1895)—Chance and the Prepared Mind," *Trends in Biotechnology* 13 (1995): 511–15, quotation on 513.

of nature," their "brilliant" colors, their rhythmic movements resembling a "peal of bells," and their singular pursuit for food through life.[8] Pasteur applied his theory of fermentation to disease theory to assert that diseases caused by living organisms could be treated by the same living organisms in an attenuated form. Attenuation of living forms was fundamental to the Pasteurian method. Pasteur asserted that his method of partial sterilization without killing the germs was successful due to the control he exercised over living forms: "I have kept from them [the microbes], and am still keeping from them, that one thing which is above the power of man to make. . . . I have kept from them life."[9] In such an enterprise, the use of live vaccines appeared both "heroic" and ubiquitously potent. This image of valiancy was associated with the vaccination campaigns of the late nineteenth century, and live vaccines became a Pasteurian dogma.[10] In 1881 Pasteur proclaimed about his anthrax vaccine, "They are living vaccines, suitable for cultivation, transferable anywhere without being altered."[11]

Pasteur and his pupils used live attenuated virus to prepare antirabic and other vaccines. Albert Calmette and Camille Guérin developed the live tuberculosis vaccine in 1908. In 1892 Waldemar Haffkine developed the first cholera vaccine in the Pasteur Institute in Paris. It was a live vaccine, which he tested widely in India from 1892 to 1896.[12] During his journey from Paris to India Haffkine killed the vaccine with carbolic acid to preserve it, and on the ship to India he even vaccinated an IMS officer with the dead vaccine.[13] But once in India, he adhered to the Pasteurian notion and reverted to using live vaccines, which, according to historians, gave his vaccination campaigns "heroic" and "adventurous" qualities.[14] Haffkine preferred live vaccines as he believed that they produced higher

8. Eliza Priestley, "The Realm of the Microbe," *Nineteenth Cent.* 29 (1891): 811–31, quotations on 811, 816, 817, and 831.

9. Quoted in Stephen Paget, *Pasteur and After Pasteur* (London: Black, 1914), 30.

10. Bornside, "Waldemar Haffkine's Cholera Vaccines" (n. 6), 408.

11. Anne-Marie Moulin, "Patriarchal Science: The Network of the Overseas Pasteur Institutes," in *Science and Empires: Historical Studies about Scientific Development and European Expansion,* ed. Patrick Petitjean, Catherine Jami, and Moulin (Dordrecht, Netherlands: Kluwer, 1992), 307–22, quotation on 309.

12. Bornside, "Waldemar Haffkine's Cholera Vaccines" (n. 6), 405.

13. Courtney Clark Manifold, "Report of a Case of Inoculation with Carbolized Anticholeraic Vaccine (Haffkine)," *Indian Med. Gazette* 18 (1893): 101–3.

14. Löwy, "From Guinea Pigs to Man" (n. 6), 298. Bornside described Haffkine's cholera vaccination campaigns with live vaccines as "heroic." "Waldemar Haffkine's Cholera Vaccines" (n. 6), 409.

immunity.[15] He showed little regard for dead vaccines since he wanted to show spectacular success with his vaccine to convince skeptical British officials.[16] This reflected how vaccines were seen during this time, as heroic, dramatic, and radical interventions. Alongside this Pasteurian faith in the living vaccine there was another emerging tradition, a predominantly British one under Almroth Wright, which used mainly dead vaccines.

Opsonins and Dead Vaccines

Wright, professor of pathology at the army medical school at Netley, Hampshire, established a highly successful and productive research group between 1892 and 1902 there. This group had a strong colonial character as most of them like Semple, George Lamb, William F. Harvey, and Lyle Cummins were training to join either the IMS or the bacteriological department of the government of India (GOI). Wright broke away from the Pasteurian practice of using attenuated viruses as he found that killed vaccines were particularly useful for inducing the formation of antibodies.[17] Wright claimed that such vaccines carried fewer risks and were easier to standardize than attenuated live cultures.[18] It was Wright who for the first time used the dead bacteria as the active constituent of his typhoid vaccine. Working with Semple in July 1896, Wright inoculated himself and his "volunteers" with different dilutions of heated cultures of typhoid bacilli and used agglutination tests to measure any enhanced immunity produced. When he came to India as the head of the Plague Commission in 1897 he experimented with this vaccine in some of the garrisons.[19] During World War I, heat-killed antityphoid vaccines prepared by Wright, Richard Pfeiffer, and Wilhelm Kolle came to be regarded as safe and dependable.[20]

15. Löwy, "From Guinea Pigs to Man" (n. 6), 299; and Bornside, "Waldemar Haffkine's Cholera Vaccines" (n. 6), 403.

16. Löwy, "From Guinea Pigs to Man," (n. 6), 300.

17. Leonard Colebrook, "Almroth Edward Wright. 1861–1947," *Obit. Notices Fell. Roy. Soc.* 6 (1948): 297–314.

18. "Sir Almroth Wright," *Brit. Med. J.* 1 (May 1947): 646–47, 647. According to Michael Worboys, this move to using dead vaccines established Wright's approach to immunity as that of a physiologist rather than a bacteriologist. Michael Worboys, "Almroth Wright at Netley: Modern Medicine and the Military in Britain, 1892–1902," in *Medicine and Modern Warfare*, ed. Roger Cooter, Mark Harrison, and Steve Sturdy (Amsterdam: Rodolpi, 1999), 77–97, esp. 88.

19. "Sir Almroth Wright" (n. 18), 647.

20. Linton, "Was Typhoid Inoculation Safe?" (n. 6), 101–33.

However, Wright had adopted dead vaccines not just for safety. In 1902 he started his work on vaccine therapy—which stressed that vaccines could be used to stimulate the natural resistance of the individual body and not just as a prophylactic agent.[21] His vaccine program was thus more for curative purposes than prophylactic.[22] The basis of this was Wright's theory of opsonization: that a patient who suffered from a particular infection had an abnormally low opsonic index,[23] in which dead vaccines became particularly useful as he believed that they could cure as well as prevent disease.[24] Wright believed that dead bacteria vaccines could be used to stimulate the natural resistance of the individual body as it could enhance the production of opsonins and patients could fight their infection more effectively.[25] Semple followed Wright in his own work on the vaccine therapy and opsonic index for his research on enteric fever in Kasauli. Following Wright, he sought to develop vaccines that could be both prophylactic as well as therapeutic. He sterilized his vaccines with 0.5 percent carbolic acid.[26]

David Semple and His Antirabies Vaccine

Semple's choice of carbolic acid was significant. An antiseptic derived from coal, carbolic acid had a peculiarly British heritage and an industrial machismo. Joseph Lister, who "championed" it,[27] saw it being used as a

21. John R. Matthews, "Major Greenwood versus Almroth Wright: Contrasting Visions of 'Scientific' Medicine in Edwardian Britain," *Bull. Hist. Med.* 69 (1995): 30–43, esp. 35–36.

22. Wai Chen, "The Laboratory as Business: Sir Almroth Wright's Vaccine Programme and the Construction of Penicillin," in *The Laboratory Revolution in Medicine*, ed. Andrew Cunningham and Perry Williams (Cambridge, UK: Cambridge University Press, 1992), 245–94, esp. 253.

23. A substance called opsonin which is present in the patient's serum.

24. This was popularized by Wright and Alexandre Besredka. See Matthews, "Major Greenwood" (n. 21); and Ilana Löwy, "'The Terrain Is All': Metchnikoff's Heritage at the Pasteur Institute, from Besredka's 'Antivirus' to Bardach's 'Orthobiotic Serum,'" in *Greater Than the Parts: Holism in Biomedicine 1920–1950*, ed. Christopher Laurence and George Weisz (New York: Oxford University Press, 1998), 257–82.

25. Matthews, "Major Greenwood" (n. 21), 35–36; and Chen, "Laboratory as Business" (n. 22), 264–66.

26. David Semple, "A Preliminary Note on the Vaccine Therapy of Enteric Fever," *Lancet* 173 (June 1909): 1668–75, esp. 1668–69. According to him, the principle of opsonic index helps "in setting in motion the machinery which elaborates the products of immunisation." Ibid., 1669.

27. Michael Worboys, *Spreading Germs: Disease Theories and Medical Practice in Britain, 1865–1900* (Cambridge, UK: Cambridge University Press, 2000), 81.

disinfectant in Carlisle for the treatment of sewage.[28] He suggested that it could be used to kill the germs before they got a footing in the body or in the wound.[29] Wright adopted the acid to kill the viruses for his vaccines, and Semple developed his own carbolized dead vaccines for typhoid in India.[30] In 1911 he used the same principle for developing his antirabic vaccines. He had started his work on rabies from Wright's premises of the opsonic stress on blood and vaccine therapy; in using the blood of an animal infected with rabies to protect other animals against the disease.[31] During 1903–4 Semple treated two hundred patients in Kasauli with antirabic serums as a preliminary to the usual vaccine treatment. Although he found good results, it was not clear whether the results were due to the serum treatment only.[32] However, by 1911 Semple had given up his work on serum therapy and was working on a more conventional antirabic vaccine. This was perhaps because he discovered that serum therapy could not work on its own and had opted for a simpler single treatment method with conventional vaccines.[33] He developed his carbolized vaccine at the CRI from the brains of rabbits deliberately infected and then killed.[34]

Semple's carbolized antirabic vaccine brought about a confluence of Pasteurian and British researches on germs and at the same time broke away from both. It departed from the Pasteurian tradition of using a dry-cord-attenuated antirabies vaccine. At the same time, his carbolized dead vaccine was no longer developed for Wright's principles of opsonins and vaccine therapy but for safety and easy transportability in a tropical country. Semple highlighted three advantages of the vaccine: It was safe in terms of postvaccinal complications: "[K]nowing that it is a dead vaccine we can dismiss any doubts as to the possibility of its producing the disease

28. Christopher Lawrence, "Lister, Joseph, Baron Lister (1827–1912)," in *Oxford Dictionary of National Biography* (Oxford: Oxford University Press, 2004), http://www.oxforddnb.com/view/article/34553 (accessed April 2, 2008); and William Watson Cheyne, "Lister, the Investigator and Surgeon," *Brit. Med. J.* 1 (May 1925): 923–26, esp. 923.

29. William Kingston, "Antibiotics, Invention and Innovation," *Res. Policy* 29 (2000): 679–710, esp. 680.

30. Semple, "Preliminary Note" (n. 26), 1668–69.

31. David Semple, "On the Preparation and Use of Antirabic Serum, and on the Rabicidal Properties of Patients after Undergoing Antirabic Treatment; Also a Note on the Blood of a Patient Suffering from Hydrophobia," *Lancet* 171 (June 1908): 1611–18.

32. Ibid., 1613.

33. David Semple, *The Preparation of a Safe and Efficient Antirabic Vaccine: Scientific Memoirs by the Officers of the Medical and Sanitary Departments of the Government of India* (Calcutta: Superintendent Government Printing, 1911), 27.

34. Ibid., 28.

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which it is intended to prevent."[35] It could be sent to distant places in the Indian empire without reducing its efficiency.[36] Third, vaccine production could be standardized. It could be produced at one central Pasteur Institute and then sent to the rest of India.[37] With his new antirabies vaccine, Semple asserted that live vaccines were a thing of past: "No person would be justified in using a living staphylococcus, or a living streptococcus vaccine, when dead vaccines prepared from these germs answer every purpose."[38] The Pasteurian logic of the ubiquity of living vaccines was now reversed. In Semple's hand, in a tropical country like India where bacteriological research was deemed ideal only in the salubrious climate of the hills where the Indian Pasteur Institutes were built by the British, carbolized dead vaccines provided a new dimension. Semple's antirabic vaccine became popular and highly acclaimed. Pardey Lukis, the director general of the IMS (DGIMS), claimed, "The Pasteur treatment of this disease [rabies], so far as India is concerned, has been revolutionized during the past few years by Semple's discovery."[39] *The Lancet* praised Semple's vaccine as "safe and efficient."[40] This seemed the ideal vaccine for India as it could be sent to different parts of the country.

Since dead vaccines appeared particularly suitable to be transferred over long distances in tropical climates, they were also considered ideal to serve an important medical and political contingency in India: decentralization of vaccine treatment. Semple's vaccine in hermetically sealed ampoules could be transported to and stored in distant places without detriment to its quality.[41] In north India the railway center at Allahabad was opened in 1924, as the first out center supplied with vaccines from Kasauli for antirabic treatment, and centers at Lahore and Rawalpindi were opened a year later. In western India, J. Morrison (assistant director, Bombay Bacteriological Laboratory) announced that the government had adopted the policy of "bringing antirabic treatment nearer the home of those who need it."[42] By 1923 carbolized antirabies vaccine was issued to

35. Ibid., 31.

36. Ibid., 29.

37. Ibid., 4. His recommended dosage was dilutions of 4 percent and 8 percent rabies virus in 1 percent carbolic acid.

38. Ibid., 1.

39. "Opportunities for Original Research in Medicine in India," *J. Roy. Soc. Arts* 65 (1917): 391–95, quotation on 392.

40. "A Safe and Efficient Antirabic Vaccine," *Lancet* 178 (July 1911): 173.

41. William J. Webster, *Rabies and Antirabic Treatment in India* (Delhi: Manager of Publications, 1946), 6.

42. Morrison to director, Bombay Bacteriological Laboratory, May 8 1923, "Anti-rabic Treatment: Opening of Additional Centres," General Department, G.D. file no. 4761 (I), ff, 5–7, Maharashtra State Archive, Mumbai, India.

various centers in north and south India. Decentralization had an impact on awareness about the disease and treatment. In 1925 the Pasteur Institute, Coonoor, reported a decrease in the number of deaths from rabies from the previous year. The number of patients at the local centers also increased.[43]

However, this shift to dead antirabies vaccines was not just an Indian or a tropical phenomenon. A similar move took place in Europe as well, but for a very different rationale. Here the main reason for the shift was that Pasteur's live vaccine was linked to a peculiar but dreaded disease, "laboratory rabies," or *rage du laboratoire*, a form of rabies apparently produced from the vaccine itself in the laboratory. Since the days of Joseph Meister, Pasteur's antirabies methods were hotly debated by scientists and antivaccinationists who claimed that his vaccines killed more people than they cured.[44] In 1886 Michel Peter presented a clearer image of "laboratory rabies" to the scientific world when he presented to the Academy of Medicine in Paris details of eleven cases where patients had died from the "poison" of Pasteur. He suggested that Pasteur's live vaccines carried the germs of rabies, famously labeling the process the "intentional inoculation with M. Pasteur's 'laboratory rabies.'"[45] Peter's critique shook the very foundation of Pasteurian vaccine, suggesting that scientists had failed to "control" the living microorganisms as Pasteur had asserted. As a result "laboratory rabies" became symbolic of Pasteurian failures. It was also used by scientists as well as historians to refer to patients who had died with signs of paralysis after receiving the Pasteur treatment.[46]

Laboratory rabies was associated with live vaccines, the keystone of Pasteur's method. The association appeared logical. A problem identified by scientists with living vaccines was that they multiplied in the body: "[T]he multiplication of a living rabies virus intended as a prophylactic vaccine would mean hydrophobia and death to the person inoculated."[47] The concern about living vaccines was of particular concern in the context of rabies as they contained nerve cells that could lead to neurological complications.[48] These fears about inoculating with living nerve cells and

43. "India," *Brit. Med. J.* 2 (October 1925): 765–66.

44. Toby Gelfand, "11 January 1887, the Day Medicine Changed: Joseph Grancher's Defense of Pasteur's Treatment for Rabies," *Bull. Hist. Med.* 76 (2002): 698–718; and Geison, "Pasteur, Roux, and Rabies" (n. 6).

45. Bryan Benjamin, "A Pasteur Institute for India," 373–74, Home-Medical, August 1894, P/4554, Asia Pacific and Africa Collections, British Library, London (hereafter APAC).

46. Gelfand, "Day Medicine Changed" (n. 44), 710.

47. Semple, *Preparation of a Safe and Efficient Antirabic Vaccine* (n. 33), 2.

48. John W. Cornwall and W. A. Beer, "On the Occurrence of Paralysis after Treatment with Antirabic Vaccine," *Indian J. Med. Res.* 13 (1926): 467; Cornwall, "Recent Advances of Knowledge in Connection with Rabies," *Indian Med. Gazette* 42 (1907): 121.

laboratory rabies took center stage at a very important forum, the First International Rabies Conference, convened by the League of Nations and held in Paris in April 1927. Directors of all major antirabies institutes of the world attended the conference, and John Taylor (director of the Pasteur Institute in Rangoon, Burma) represented India.[49]

Fear of the Living

The conference was the finest hour of Semple's vaccine. The discussion centered around methods of treatment and accidents from antirabies treatment worldwide.[50] In his presentation Taylor showed statistics for all the Indian Pasteur Institutes, around 170,000 cases, which easily outnumbered those of any other country. In India the cases were also much more severe.[51] Most importantly, Taylor showed that paralytic accidents hardly occurred with carbolized dead vaccines.[52] The dead carbolized vaccine now appeared to be the new hope for Europe.

The Indian antirabic experience received high commendation even from the core Pasteurian group. A. C. Marie, professor at the Pasteur Institute in Paris, found the results obtained by Semple's method to be "most significant."[53] Paul Remlinger, director of the Pasteur Institute in Morocco, who analyzed postvaccinal paralytic cases in all Pasteur Institutes of the world using various methods, found Semple's method to be the safest and considered that "the elucidation of this fact appears to us to be the most important lesson provided by the Conference"[54] (Table 1).

The conference also concluded that the dead carbonized and etherized vaccines were best suited for large-scale production with the growing popularity of antirabies vaccination throughout the world.[55] The resolu-

49. H. G. Dennehy to Under Sec of State, December 9, 1926, Economic and Overseas Department Papers, L/E/7/1465, 1, APAC.

50. J. Taylor, "Note on the International Rabies Conference Held in Paris April 1927," 3, ibid.

51. Ibid., 4.

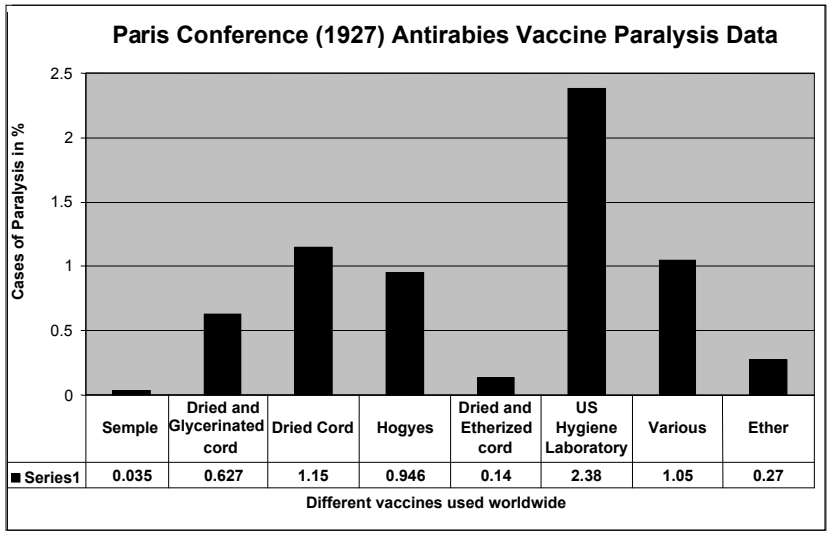
52. Ibid., 6.

53. A. C. Marie, Paul Remlinger, and H. Vallée, *International Rabies Conference Held at the Pasteur Institute, Paris, from April 25th to 29th, 1927* (Geneva: League of Nations, 1927), 48.

54. Ibid., 97–98. Remlinger's own work was mainly on the paralytic accidents from rabies; see George M. Baer, ed., *The Natural History of Rabies* (New York: CRC Press, 1991), 15–16; Remlinger, "Accidents paralytiques au cours du traitement antirabique," *Ann. de l'Inst. Pasteur* 19 (1905): 625; "Rage experimentale de la souris et du rat," *C.R. Soc. Biol.* 56 (1904): 42; and "La rage de laboratoire," *Bull. Acad. Med. Paris* 113 (1935): 836.

55. "Anti-rabies Vaccination and the Public Authorities," in Marie, Remlinger, and Vallée, *International Rabies Conference* (n. 53), 154–57.

Table 1. Paris conference (1927) worldwide antirabic vaccine paralysis data.



Source: A. C. Marie, Paul Remlinger, and H. Vallée, International Rabies Conference Held at the Pasteur Institute, Paris, from April 25th to 29th, 1927 (Geneva: League of Nations, 1927), 83–84.

tions passed at the conference supported dead vaccines, carbolized following Semple's method and etherized as done more recently by Adolph Hempt.[56] The conference also resolved that comparative tests on a large scale should be carried out in certain selected institutes with the two vaccines. Kasauli was to be one of such sites.[57] Under Secretary of State for India Edward J. Turner received Taylor's report warmly in London and forwarded it to Delhi, suggesting that the GOI should publish a summary of it in Indian medical journals.[58]

Matters in India, however, seemed to be on a somewhat different note. In the face of this enthusiasm about the dead carbolized vaccine in London, the public health commissioner (PHC) for India, J. D. Graham, wrote to the India Office (London) recommending "against [the] immediate publication of Taylor's report . . . in view of certain local factors."[59] In his

56. Marie, Remlinger, and Vallée, *International Rabies Conference* (n. 53), 7.

57. Ibid., 8.

58. Edward J. Turner to the Sec, Govt of India, July 15, 1927, 6, Economic and Overseas Department Papers, L/E/7/1465, APAC.

59. "Extract from Private a Letter from Col. Graham to Mr Donaldson," 22 September 1927, ibid.

subsequent note Graham added that despite the sanction from Europe, in India the carbolized dead vaccine was not considered the final word, and at the Pasteur Institute in Kasauli the director, John Cunningham, was involved in comparative tests with etherized and carbolized vaccines, which was one of the recommendations of the Paris conference.

However, in Kasauli, Cunningham was in fact experimenting with live vaccines attenuated by ether, contrary to the Paris resolutions, which recommended using dead vaccines, etherized or carbolized.[60] The rationale for Cunningham's research was different as well from the Paris resolutions. To defend his project he had invoked the old Pasteurian doctrine of the potency of live vaccines, suggesting that the Indian Pasteur Institutes faced much greater numbers of severe cases than those in Europe and therefore required a more potent live vaccine.[61] At the same time he asserted the autonomy of Indian scientific research from European trends: "India must work out her own antirabic problem without too much slavish deference to European ideas."[62] Although the Paris resolutions had instructed experimentation on two types of dead vaccines, etherized and carbolized, Cunningham in Kasauli had created his own divide between the live and the dead, that between etherized and carbolized, and had adopted the former as a live vaccine.

This new development had an immediate implication for the antirabies vaccination policy of the GOI. The ongoing decentralization of rabies treatment had to be stopped as Cunningham insisted that all patients needed to be sent to Kasauli to facilitate the experiments on a large scale.[63] This exposed the contrasting political interests involved in vaccination policy in India. The India Office in London, keen to highlight the success of vaccine research and vaccination in India, internationally and to the British public, reacted strongly to this change. The Under Secretary of State Arthur Hirtzel wrote to the GOI that he was unable to understand why authorities in India still wanted to continue the experiments, centralize research, and send all the patients to the remote hills when a safe and acclaimed vaccine was available. This would mean that many patients could die without treatment: "[T]he suggestion seems to me to confuse means & ends. After all, human life is something, even in India!"[64] The India Office was sensitive about human experimentations in India due to the pressures of British antivivisectionists and humanitarians who kept a

60. Graham to Donaldson, New Delhi, November 16, 1927, 2–3, ibid.
61. Ibid., 5.
62. Quoted by Graham, ibid., 3.
63. Ibid., 4–5.
64. Arthur Hirtzel (Under Sec of State) to the Medical Adviser, January 17, 1928, ibid.

keen eye on the activities of the Indian Pasteur Institutes. Laboratories and medical experiments in the colonies were sensitive issues in London, a sensitivity that authorities in India did not always share.[65]

Scientific opinion in India too was firmly in support of the Semple vaccine.[66] Directors of the other Indian Pasteur Institutes who had already made plans for decentralization and mass inoculation with the Semple vaccine were skeptical of Cunningham's experiments in Kasauli. John Morrison, director of the Shillong Institute, wrote to Smith (the medical advisor in London) about the "human side" of the question, that lack of treatment in remote areas would lead to high mortality, a factor that those making policy from Shimla had "not done justice to."[67] He enclosed transcripts of debates at the Assam legislative assembly that highlighted the growing pressure on the institutes and the provincial government to decentralize treatment.[68]

However, the elite group in Shimla, comprising influential medical personnel of the GOI, had a different point of view. Even before the Paris conference, a decision was taken by the GOI to stop decentralization of rabies vaccination in light of Cunningham's new experiments in Kasauli. In 1925 the Indian PHC reported that Cunningham would undertake experiments with the etherized vaccine in Kasauli and "pending the results . . . no new centres, military or civil, should be established in the plains."[69] In September 1926 a Medical Committee comprising T. H. Symons (DGIMS), Graham (PHC), John K. S. Fleming (deputy DGIMS), S. R. Christophers (director, CRI, Kasauli), and Cunningham (director, Pasteur Institute, Kasauli) met in the office of the DGIMS in Shimla.[70] They decided that no new centers were to be opened to facilitate Cunning-

65. Pratik Chakrabarti, "Beasts of Burden: Animals and Laboratory Research in Colonial India," *Hist. Sci.* 48 (2010): 125–51.

66. William F. Harvey and H. W. Acton, "An Examination into the Degree of Efficacy of Antirabic Treatment," *Indian J. Med. Res.* 9 (1923): 853; R. Knowles, "Some Problems in Rabies," *Indian Med. Gazette*, 67 (1927): 389–91.

67. Morrison to Smith, January 10, 1928, Economic and Overseas Department Papers, L/E/7/1465, APAC.

68. "Extract from Official Report of the Assam Legislative Council Debates," April 9, 1928, 482, ibid.

69. *Annual Report of the Public Health Commissioner with the Government of India,* 1925, vol. 1, 61–62, V/24/3659, APAC.

70. "Minutes of a Meeting of a Medical Committee held in the office of the Director-General, Indian Medical Service, on September 28 at 11 am, 'Inadvisability of Extending Anti-rabic Treatment by Present Carbolised Vaccine to District Areas in India until Results of Investigations Are Known,'" Department of Education Health and Land, Medical Branch, 1926, 95–96 B, 6, National Archive of India, New Delhi (hereafter NAI).

[34.230.35.103] Project MUSE (2024-03-28 12:46 GMT)

ham's experiments with live vaccines. They also anticipated that the forthcoming conference in Paris with its strong Pasteurian legacy would pronounce emphatically in favor of the etherized live vaccines.[71] At this stage this group in India underestimated how much the fear of paralysis and the living vaccine had gripped contemporary European scientific opinion. But the question remains, why then did the GOI send Taylor to Paris with the positive results of the Semple vaccines? To understand this, we have to focus closely on the ongoing experiments in Kasauli under Cunningham.

The Revival of the Live Vaccine

John Cunningham (Figure 1) was a Scottish physician who joined the IMS in 1905 and after working in various laboratories in India served as director of the King Institute in Madras (1919–26) and that of the Pasteur Institute in Kasauli from 1926.



Figure 1. John Cunningham. Source: Edinburgh University Library, Special Collections Department, "John Cunningham in Brewery Garden," Kasauli 1916, Gen 2004 B.5 XX/3, JC papers (n. 73).

71. Ibid., 6–7.

Anderson G. McKendrick (1876–1943), another IMS officer and a friend, who was then working at the Edinburgh Research Laboratory, introduced Cunningham to etherized vaccine in 1925.[72] McKendrick was the director of the Pasteur Institute at Kasauli between 1914 and 1920, when he concentrated on rabies research. In Britain, he subsequently became an authority on rabies. He was also a delegate at the rabies conference in Paris.

McKendrick was keen that Cunningham should try the new ether method developed by Hempt and G. P. Alivisatos, perhaps to serve his own interests in collecting statistics on antirabies vaccination. Throughout the 1920s he collected and compiled data about various antirabic methods used in different institutions worldwide. Soon after Cunningham joined PIK as director, McKendrick sent him a survey of recent literature encouraging him to try the new ether method.[73] McKendrick himself expressed no particular preference for either ether or live vaccines. At the Paris conference he expressed the view that there was no significant difference in terms of mortality among Pasteur's original dried cord, Hoyges's dilution, and Semple's carbolized vaccines.[74]

While McKendrick was interested in the new ether method for collecting statistical data, Cunningham adopted the etherized vaccine with new enthusiasm and conviction. He believed in the orthodox Pasteurian dogma that a live vaccine had greater potency and felt it was ideal for severe Indian cases. He came to this conclusion particularly after reading Hempt's early publications.[75] Soon after becoming the director of PIK, Cunningham started his experiments with etherized vaccines with patients with the most severe injuries.[76] He informed Graham about the new ether method and added that although in India dead carbolized vaccine had been adopted, institutes in Europe were "using virus which is not dead but attenuated by ether."[77]

72. McKendrick was a mathematician, epidemiologist, and army officer belonging to the IMS, director Pasteur Institute, Kasauli (1914–20). He also served as the superintendent of the Research Laboratory, Royal College of Physicians, Edinburgh (1920–41).

73. McKendrick to Cunningham, December 13, 1925, E. 15, Papers and correspondence of John Cunningham, 1880–1968, reference code: GB 0237 Gen. 2004, 15 boxes, Special Collections, Edinburgh University Library, Edinburgh (hereafter JC papers).

74. "Further Note on the Antirabic Treatment Position," L/E/7/1465, 1–6, APAC.

75. "Notes on Literature on Rabies," A. 14, JC papers.

76. Ether Experiments, I, Resistance to Ether 1926–1927, E. 3, Ether Experiments, III. Human Cases Treated with Ether Virus, 1926–7, Note 8, October 1926, "It has been decided to treat the worst human cases attending the Institute with ether vaccine." E. 5, JC papers.

77. Cunningham to Graham, copy to John K. S. Fleming, secretary, Pasteur Institute of India, January 22, 1926, E. 15, ibid.

Cunningham's preference for ether was as significant as Semple's choice of carbolic acid. The two attenuating agents had distinct historical trajectories. While carbolic acid was an antiseptic from Carlisle with a Listerian tradition, ether was an anesthetic with a Pasteurian lineage.[78] It was originally used by Pasteur for his rabies vaccine experiments and then by Remlinger and Roux.[79] To Cunningham, ether seemed to have a special characteristic: "[T]reatment with ether removes the toxic substance, which is responsible for post treatment paralysis."[80]

Soon after he started, Cunningham received news of a suspicious death of a British subaltern named Norman following treatment with carbolized vaccine.[81] His laboratory notes show reports of several more patients suffering from similar postvaccinal paralysis.[82] This led him to express his doubts to Graham. He now wanted to begin large-scale experiments with the ether-attenuated virus and also centralization of vaccination in his laboratory in Kasauli.[83]

Cunningham was also suspicious of evidence of the early success of carbolized vaccine in Indian institutes. He wrote to Graham that he could not find any original report of Semple's experiments in Kasauli.[84] After searching in Shimla Graham found some confidential notes about the original experiments of 1911–12 conducted in Kasauli, which were, as he wrote to Cunningham, "extremely interesting reading" and that "paralytic complications ensued from time to time."[85]

Cunningham reported this to H. W. Acton (director of the Calcutta School of Tropical Medicine) and the new evidence with Semple's vaccines that he had come across where even 1 percent carbolized vaccines caused paralysis.[86] He also wrote to Fleming (deputy DGIMS and secretary of the Pasteur Committee of India) challenging the policy of decentralization by using carbolized vaccines: "No one can claim, however, that carbolised vaccine . . . is the last word in antirabic treatment."[87] He pointed out that

78. The colorless, light, volatile liquid ($C_4H_{10}O$) resulting from the action of sulfuric acid upon alcohol.

79. Lise Wilkinson, "The Development of the Virus Concept as Reflected in Corpora of Studies on Individual Pathogens. 4. Rabies—Two Millennia of Ideas and Conjecture on the Aetiology of a Virus Disease," *Med. Hist.* 21 (1977): 15–31, esp. 29.

80. Cunningham to Graham, January 22, 1926, E. 15, JC papers.

81. W. Keyworth to King, Mardan, March 3, 1926, E. 6, ibid.

82. Patient postcard to the director, Pasteur Institute, Kasauli, January 14, 1926, ibid.

83. Cunningham to Graham, March 2, 1926, ibid.

84. Cunningham to Graham, August 26, 1926, E. 15, ibid.

85. Graham, Office of DGIMS to Cunningham, September 14, 1926, ibid.

86. Cunningham to Acton, November 3, 1926, ibid.

87. Cunningham to Fleming, September 16, 1926, ibid.

recent work in Europe by Alivisatos, Hempt, and Busson with etherized vaccines had shown better mortality rates. According to Cunningham, the etherized vaccine was live and needed to be prepared every day in the laboratory, which required the treatment to remain centralized.

The issue of centralization reflected an important character of medical research in British India. Imperial medical research in India commenced in the isolated hill-top laboratories. Cunningham's project provided a new impetus to the logic of medical research in the Indian Pasteur laboratories, which were developed as elitist and rarefied imperial institutions far from the bustling and clamorous tropical plains. Cunningham believed that with the impending decentralization, the Indian Pasteur laboratories would become redundant: "[A] very important duty of the Government of India to see that such an Institute does exist where new methods can be tested and antirabic research carried on. For this purpose a certain number of patients to be treated is a necessity and the total cessation of such cases would immediately put the Institute out of touch with the most important side of antirabic world."[88] Therefore, the opposition to decentralize was not just to test live vaccines but also to retain the Pasteur Institute as the experimental and imperial headquarter of medical research in India. This provided a new rationale to the GOI to sustain the remote Pasteur Institutes, a policy that increasingly came under criticism from Indian nationalists.[89]

Cunningham's plans and experiments with the etherized vaccines, however, soon received a setback. In January 1927 he was informed that *dafadar* (Indian cavalry) Kalyan Singh developed severe paralysis after being treated by etherized vaccine at Kasauli. The civil surgeon treating him reported his horrific death to Cunningham: "The patient was lying propped up on pillows with flushed face upon which was an expression of anxiety and fear" and added that he had suffered from "complete flaccid paralyses."[90] Cunningham came across other similar cases that he reported to Fleming but was careful not to link them to the dreaded "laboratory rabies": "The first point to make clear is that this was not a case of 'rage laboratoire.'"[91] He suggested that the paralysis was due to foreign nerve tissue and was common in all antirabic treatment. But his firm faith in the

88. Cunningham to the Secretary, Pasteur Institute of India, September 1, 1926, 1–8, ibid.

89. David Arnold, *Science, Technology and Medicine in Colonial India* (Cambridge, UK: Cambridge University Press, 2000), 199.

90. Civil surgeon, Jodhpur to Cunningham, January 27, 1927, E. 6, JC papers.

91. Cunningham to Fleming, January 4, 1927, 1–4, E. 15, ibid.

ether vaccine had been shaken, and he suggested a tactical retreat, that ether vaccines should be used in Kasauli only for severe cases.

In February 1927 Cunningham was faced with the forthcoming Paris conference, when the complications with the etherized vaccine became known. He wrote to McKendrick requesting his support at the conference.[92] Cunningham had one more important revelation to make to McKendrick. He had found that the original fixed virus with which he worked in Kasauli was so weak that it actually died when immersed in ether and could not be attenuated as done by Hempt and Alivisatos in Europe. In effect, he had experimented with a practically dead etherized vaccine.[93] This meant that he could not really suggest the advantages of a live etherized vaccine apart from the fact that even the dead etherized vaccine led to paralysis. Therefore, at the time of the Paris conference Cunningham was in an ambiguous position and did not send any details of his experiments. He hoped that the conference would vote in favor of the new European etherized vaccine so he could continue his research.

"Living versus Dead"

The Paris conference led to a period of intense experiments by Cunningham in his remote Kasauli laboratory with live vaccines amid growing domestic and international scientific and political pressures, which favored dead vaccines. The developments of the three years 1927–29 shaped the final configurations of the vaccine and also the future of Indian antirabies vaccination policy. As we shall see, despite clear positioning among scientists about live and dead vaccines, there remained a range of ambiguity about live and dead vaccines. This was particularly due to the fact that there were several variables involved in the production of vaccines, like the strength of the *virus fixe*, the time and degree of attenuation, and the nature and strength of the attenuating agent. Thus, in Kasauli following the methods of Hempt and Alivisatos for preparing a living etherized vaccine, Cunningham found his vaccine to be dead. In Pasteurian research, categories like dead and living were used as moral claims and prejudices. No consistent scientific category or experimental method was defined to distinguish one from the other, which were essentially *differences in degrees of attenuation.*

92. Cunningham to McKendrick, February 9, 1927, 3–4, E. 15, ibid. Cunningham also wrote to McKendrick that although Taylor, who was on leave in England, was to represent India, "[h]e does not know the ins and outs of the matter as far as Kasauli is concerned, however, and so you will have to stand up for our opinions there." Ibid.

93. Ibid.

McKendrick clearly had a difficult task in Paris. On one side were the Pasteur hardliners like Roux and Calmette who still favored the original dry cord method and live vaccines; on the other were the new breed of scientists convinced of the benefits of the dead carbolized and etherized vaccines. He found the conference divided in two camps; as he wrote to Cunningham, "[T]he question is living versus dead."[94] In the debates there the etherized vaccine was clearly considered dead, as he wrote that the new trend was to develop vaccines that were "[d]ead including both carbolized and etherized. . . . Kill by any means and get the results."[95] After a chat with Hempt, McKendrick realized that Hempt too had turned toward dead vaccines to avoid cases of postvaccination paralysis.[96] But he rejoiced at the fact that the original dry cord method of Pasteur received a decisive blow due to postvaccinal paralysis. Even those working in the Paris Institute now seemed to prefer dead vaccines for the fear of paralysis: "[I]t is dead vaccine that all are striving after though they may not admit it."[97] The Pasteurian Remlinger seemed to be torn between two worlds; in his researches in Morocco he had come across several cases of paralysis with dried cord vaccines and yet faced the Pasteurian hardliners in Paris who insisted on the original method: "Remlinger looked to me like a soul in purgatory. His reason and his sentimentality were pulling in different directions."[98]

Back from the conference McKendrick reminded Cunningham that there was an open field to make important contributions from the massive experiments possible in India: "[W]hen the next conference comes on, say in 3 or 4 years. . . . From the international point of view India stands in a unique position from its experience of this one disease 'Rabies.' Rabies may not be economically as important to India as say Malaria. But regarding Malaria India is a small unit, regarding Rabies India stands out prominent. Think that over. You cann't [*sic*] afford to neglect the shop window."[99]

India provided the scope to define the new dead vaccine, etherized or carbolized. Cunningham interpreted this as encouragement to continue his research with live etherized vaccines. He had retained his faith and fascination with the living vaccine, something he had actually not been able to experiment with owing to the weakness of the Kasauli strain. He

94. McKendrick to Cunningham, May 11, 1927, 5, E. 16, ibid.
95. Ibid.
96. Ibid., 2–3.
97. Ibid., 2–3.
98. Ibid., 4.
99. Ibid., 5.

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noted that the French scientists still believed that living vaccines, although hazardous, were more potent and decided that that is where his future contribution in antirabies research would be, particularly for India where cases were much more severe.[100] This is how he arrived at a position so contradictory to the Paris resolutions in 1927.

Following the conference, Cunningham resumed his comparative researches on live and dead vaccines (Figures 2 and 3). Now he could also start experiments with the fresh fixed virus sent by Calmette from Paris, which seemed to remain alive after being etherized. His experiments with the two methods were in favor of Alivisatos, in terms of mortality rates (Table 2). Two facts are evident from Table 2. First, even the so-called living vaccines showed figures of mortality. Second, the better results were with Alivisatos's method, which contained larger quantities of brain substance than Hempt's.[101]

Table 2. Cunningham's experiments with live vaccines, 1927: Hempt and Alivisatos.

Methods	Total treated	Total death	Percentage deaths
Alivisatos	169	4	2.3
Hempt	66	4	6.0
Total	235	8	3.4

Source: Cunningham, "Note on the Present Position of Antirabic Treatment with Reference to the Policy To Be Adopted in the Future," August 18, 1927, 13–14, E. 17, JC papers (n. 73).

While Cunningham was conducting his experiments in Kasauli he received correspondences from scientists in Europe interested in the Semple vaccine. In August 1927 Carl Prausnitz (1876–1963, German bacteriologist), who was impressed by the success of the carbolized vaccine at the Paris conference, wrote to Cunningham about his decision to change his own treatment to the Semple method.[102] He was therefore surprised to learn that in Kasauli Cunningham had reverted to using live etherized vaccine, particularly when Hempt himself, following several cases of paralysis, had moved to a dead carbolized one.[103] It was at this point that Cunningham admitted to Prausnitz that he had not known about the

100. Cunningham to McKendrick, July 1, 1927, ibid.
101. Ibid., 15.
102. Carl Prausnitz to Cunningham, August 19, 1927, E. 18, ibid
103. Prausnitz to Cunningham, October 24, 1927, ibid.



Figure 2. Preparation of Alivisatos' vaccine in Kasauli. The weighed brain was placed on a square of mosquito netting, the four corners of which were caught up in a glass hook. It was then suspended in ether. Source: Wellcome Library, London, image V0030195.

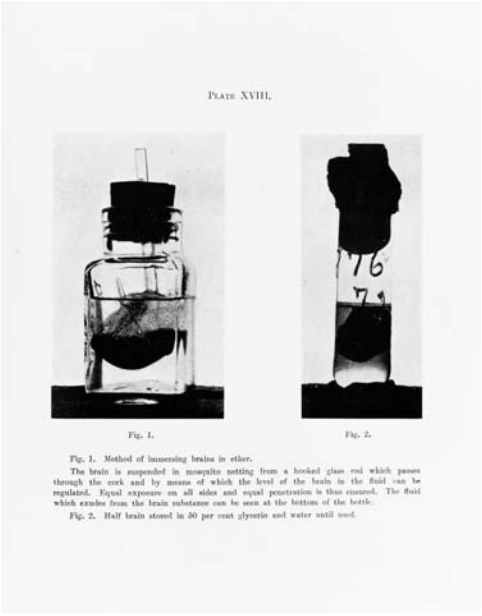


PLATE XVIII.

Fig. 1. Fig. 2.

Fig. 1. Method of immersing brains in ether.

The brain is suspended in mosquito netting from a hooked glass rod which passes through the cork and by means of which the level of the brain in the fluid can be regulated. Equal exposure on all sides and equal penetration is thus ensured. The fluid which exudes from the brain substance can be seen at the bottom of the bottle.

Fig. 2. Half brain stored in 50 per cent glycerin and water until used.

Figure 3. Immersed brain matter in ether, Kasauli. Source: J. Cunningham, M. J. Nicholas, and B. N. Lahiri, "The Action of Ether on the Rabies Virus," in *Far Eastern Association of Tropical Medicine: Transactions of the Seventh Congress Held in British India* (Calcutta: Thackers Press, 1927), 531–36, 532. Source: Wellcome Library, London.

change made by Hempt, although he had clearly learned about it previously from both McKendrick and Taylor.[104]

Cunningham now accepted that Hempt used dead vaccines as he had found a new hero in Alivisatos, who had apparently not made the shift to dead vaccines. From here on Cunningham was more inclined to use the Alivisatos method for severe cases. He also refused to use dead carbolized vaccines of higher dosage as suggested by others. Instead he now insisted that the Indian cases had peculiarities that required a different vaccine, insisting ironically that the Semple vaccine was more suited for European conditions than for India: "[C]onditions in India are so different to those in Europe that the principles laid down in my August note as to the possibility of using living virus in certain cases still holds good."[105] Later that year, Cunningham sent another report to the League of Nations where he elaborated the same problem with the new dead vaccine, which required much more brain substance, leading to paralytic cases. His preference was for live vaccines of lower dosage.[106] He also elaborated that while scientists in Europe were trying to standardize dosage for all cases, in Kasauli they had adopted a method of classification, giving the high dosage in only severe cases.[107]

The results of these experiments were presented at the Rabies Conference in Calcutta in December 1928, where directors of all the Indian Pasteur Institutes met to discuss the future of antirabic policy for India. Cunningham presented the results of his experiments with etherized vaccines and remained opposed to increasing the dosage of carbolized vaccine. He suggested a combination of treatment, etherized living Alivisatos vaccine for more severe cases and carbolized for others. He also opposed any decentralization.[108] He faced severe opposition from other directors. William C. H. Forster, president of the Central Committee, Pasteur Institute Burma, stressed the immediate need for out centers.[109] The terrain of a province like Burma made it impossible for patients to travel to Ran-

104. Cunningham to Prausnitz, February 10, 1928, 1–2, ibid.

105. Cunningham to Graham, January 31, 1928, 1–4, ibid.

106. Report by Cunningham to the League of Nations, "Note on Para 2 Letter of July 14th 1928 from the Medical Director, League of Nations, to the Public Health Commissioner with the Govt of India, Dealing with Resolution No. 11.5 of the International Rabies Conference 1927," 3, E. 19, ibid.

107. Ibid., 4. The Semple vaccine was standardized later, even in India, into a single dosage.

108. "Provisional Agenda for Rabies Conference to be Held at Calcutta on 21st December 1928," 3, ibid.

109. W. H. C. Forster, "A Note on the Present Position of Anti-Rabic Treatment in India" 1, ibid.

goon, leading to higher mortality in the provinces. While mortality among Rangoon patients was 0.37 percent, that among up-country patients was 1.07 percent.[110] In severe cases, the mortality rates were 1.08 percent and 5.07 percent, respectively. [111]

In the middle of these experiments and debates, there was an abrupt end to Cunningham's pursuance of antirabic research in India. In February 1929 he left India and went on leave to Edinburgh. R. H. Malone, who had assisted him in his researches, took over the investigations.[112] In 1929 Malone produced the first report with results of the experiments undertaken by him and Cunningham, which showed that Alivisatos (the now live vaccine, according to Cunningham and Malone) gave better results than the 5 percent carbolized vaccine, which was in turn better than the 5 percent E.C. (etherized–carbolized, Hempt).[113] Cunningham forwarded a copy of the report to Graham and dismissed the opinion of the other directors: "Their opposition simply means that our suggestions do not fit in with their preconceived ideas."[114]

However, pressure for decentralization with the carbolized vaccine in India was mounting. In December 1929 a Medical Research Workers Conference was held in Calcutta where the Rabies Committee, consisting of the directors of other Indian Pasteur Institutes like Acton, King, and Taylor, examined an interim report submitted by Malone and Cunningham. This report provided a more substantial comparative analysis of Hempt, Alivisatos, and Semple vaccines of 5 percent and 2 percent strengths on humans (see Table 3).[115]

So while Alivisatos (live) and Semple (carbolized) showed similar results, Hempt's etherized–carbolized (*very dead*) vaccines showed the worst mortality rates. One point to note is that in these statistics again, and in all the subsequent ones, the paralytic cases were ignored altogether. In India mortality and severity of bites seemed to have dominated the research questions.

There is a need to ask the question, what was a live and what was a dead vaccine? In attenuating terms, such categorization between dead

110. Ibid.

111. Ibid., 2.

112. Cunningham to Secretary, Scientific Advisory Board, Indian Research Fund Association, January 10, 1929, E. 20, ibid.

113. Malone to Cunningham, August 29, 1929, E. 21, ibid.

114. Cunningham to Graham September 19, 1929, ibid.

115. "An Investigation into the Comparative Values of Carbolised and Etherised Vaccines in Antirabic Treatment," Malone's Interim Report, prepared December 13, 1929, 7–8, E. 21, ibid.

Table 3. Comparative analysis of Hempt, Alivisatos, and Semple vaccines on humans.

Severity of cases	Vaccine employed	Dosage	Total nerve substance (in grams)	Duration of treatment (in days)	Mortality
IV	5% carbolized 5% etherized-carbolized 5% etherized (Alivisatos) living	According to Alivisatos method described in the first report	From 8.5 to 3.4 according to weight	15	4.90 5.38 4.88
III	5% carbolized 5% etherized-carbolized 5% etherized (Alivisatos) living	According to the method described in the first report	From 4 to 1.6 according to weight	15	0.81 1.07 0.54
II	2% carbolized 2% etherized-carbolized	5 cc for first 3 days; 10 cc for last 4 days	1.1 for all cases	7	
I	2% carbolized	5 cc for 4 days or 5 cc for 7 days	0.4 or 0.7	4 or 7	

Source: Malone-Cunningham, 1929, E. 21, JC papers (n. 74), 7–8.

and living vaccines, however, remained vague and often indistinguishable. While undertaking these different methods of producing vaccines and experimenting with them, Malone identified an interesting phenomenon: the line between the live and the dead was not always clear. While Semple claimed that the virus in 8 percent suspension of brain was dead after incubation at 37°C for twenty-four hours in the presence of 1 percent carbolic acid, "but we have shown that it is not the case, for if sufficient number of rabbits be subdurally inoculated with 0.2 c.c. of such suspensions approximately 1 in every 125 will contract rabies and presumably a greater number would have been infected had we been able to inoculate larger quantities."[116] So by this definition, even the Semple vaccine contained live viruses that could infect patients. Malone confirmed that the good results with 5 percent carbolized was due to higher nerve cell content, but even in this vaccine "the possibility of the presence of living virus in the 8 percent suspension from which the vaccines were prepared cannot be entirely excluded." Even earlier, in 1926, Cunningham found that the Kasauli fixed virus died if immersed in ether for thirty-six hours.[117] But in 1927, when he studied the action of ether on Indian "street virus" (that collected from infected dog brains sent recently), the virus remained alive in central portion of the brain immersed up to seventy-two hours.[118] Finally in 1928 he discovered that living virus could be found in infected brains after immersion in ether up to eighty-four hours, but not in cords exposed to ether for ninety-six hours.[119]

Even in 1929 Malone had written to Cunningham that he was struck by the fact that the "number of brains which contained live virus after immersion in ether is greater than the number shown because we have not retested the original brains when the first passage animals have died without symptoms of rabies."[120] He also referred to the same confusion that he mentioned in the report: "[T]he 8% carbolised vaccine is also attenuated and not dead as supposed by Semple."[121] Despite these doubts, he maintained the conventional distinctions between dead and living vac-

116. Ibid., 18–19.

117. John Cunningham, M. J. Nicholas, and B. N. Lahiri, "The Action of Ether on Fixed Virus," *Indian J. Med. Res.* 14 (1926): 505–20, esp. 505.

118. Cunningham, Nicholas, and Lahiri, "The Action of Ether on 'Street Virus' in Infected Brains," *Indian J. Med. Res.* 15 (1927): 85–88, esp. 85.

119. Cunningham, Nicholas, and Lahiri, "The Action of Ether on Street Virus on Infected Cord," *Indian J. Med. Res.* 16 (1928): 245–51, esp. 245.

120. Malone to Cunningham, April 11, 1929, E. 9, JC papers.

121. Ibid.

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cines in the final report and recommended the Alivisatos method, which supposedly used live vaccines.[122]

Other directors of Indian Pasteur Institutes remained strongly opposed to the employment of a live vaccine.[123] They pointed out that according to Malone's report, while in 1925 the total brain substance used was 0.7 to 1.95 grams, leading to a mortality of 1.07 percent, in 1926–27, when the total brain matter used was 0.7 grams, mortality had risen to 1.39 percent. From this they drew the conclusion that the real difference in the mortality rate was due to the quantity of brain substance and so the improvements in the vaccines should be on those lines, rather than using a live one.[124] They also highlighted that for millions of Indians affected by rabies it was better to give them a "stable" vaccine like Semple's than a "freshly prepared non-stable vaccine containing a living virus." In its final resolutions the committee "condemned" the use of a live vaccine and stressed that the dead carbolized vaccine should be adopted. It also recommended an increase in dosage for severe cases.[125] The policy of decentralization was supposed to be based on geographical and human factors rather than laboratory requirements.[126] These recommendations and resolutions were subsequently adopted by the GOI and the local governments as the official Indian antirabies policy.

The Making of the Semple Vaccine

Antirabic researches soon stopped at the Pasteur Institute in Kasauli. In 1931 Malone was transferred to Rangoon as the officiating director of the

122. "An Investigation into the Comparative Values," E. 21, 19, ibid.

123. Malone to Cunningham, January 9, 1930, E. 21, ibid. Stuart and Krikorian worked in the Department of Health Laboratories in Palestine where they conducted experiments on both etherized and carbolized (both killed in their opinion) vaccines and concluded that the Semple vaccine reduced cases of paralysis. G. Stuart and K. S. Krikorian, "Studies in Antirabies Immunisation," *J. Hygiene* 29 (1929): 1–34; "Appearance and Persistence in Rabbits' Blood of Rabicidal Antibodies Produced by Various Methods of Anti-rabies Immunisation," *J. Hygiene* 31 (1931): 414–22; and "The Rabicidal Antibody Content of Rabbit Immune Serum as an Index of Acquired Resistance to Rabies Infection," *J. Hygiene* 32 (1932): 489–93.

124. "Observations by the Directors of Pasteur Institutes of India on the Report by Cunningham and Malone Entitled 'An Investigation into the Comparative Values of Carbolised Vaccine and Etherised Vaccines of Alivisatos and Hempt in Anti-rabic Treatment' Carried Out at the Pasteur Institute, Kasauli," E. 21, JC papers.

125. "Summary of the Recommendations by Rabies Committee Convened in December 1929, during the Research Workers Conference at Calcutta, Together with a Copy of Resolution No. 7, Relating to Anti-rabic Treatment in India," Department of Education Health and Land, Health Branch, 1930, 341–44 B, 5, NAI.

126. Ibid., 5–6.

Pasteur Institute there. In 1939 the Pasteur Institute in Kasauli was closed down entirely and all its routine work was transferred to the CRI.[127] The final report of this project was drawn up by H. E. Shortt at Kasauli, in the absence of both Cunningham and Malone (Table 4).[128]

The report clarified for the first time, that the main variable element in the vaccines was the quantity of brain matter: "[T]he better result recorded with the 5 per cent vaccines, whether carbolized or etherized, is primarily due to the increased dose of brain substance administered and not to either the presence of living virus in the vaccine or the preliminary treatment of the brain with ether."[129] It should be added that in all these statistics, like in the earlier ones, the cases of paralysis were not mentioned at all. In India mortality and severity of bites dominated research questions rather than safety. One observation to make here is that quantities of brain matter and degrees of attenuation remaining the same, the results were similar. The etherized–carbolized vaccine showed worst results as it was much more attenuated. To that extent the Paris question about live and dead vaccines now seemed a nonissue. However, this did not erase the conventional divides between dead and living vaccines.

By the 1930s the general emphasis of antirabic vaccine research shifted from the type of vaccine to the dosage. A report in 1934 by Shortt, Malone, and A. C. Craighead pointed out that "the improvement recorded as a result of the introduction of the method of Alivisatos was due not to any inherent value of the precise details of the method but to the fact that it utilized a larger total dose of brain substance. Thus the use of a carbolised 5 per cent rabbit vaccine gave results comparable with Alivisatos's vaccine."[130] It concluded that "[t]he advantage of a higher dosage of brain substance . . . thus been established."[131] The *British Medical Journal* (*BMJ*), while commenting on the 1933 report, considered even Alivisatos's vaccine as dead, along with the Semple and Hempt vaccines, as according to it only dried cord vaccines were living ones.[132]

As a consequence of this consensus, by the late 1930s the dosage of the Semple vaccine was increased and standardized. The vaccine now contained

127. Webster, *Rabies and Antirabic Treatment* (n. 41), 6.

128. "An Investigation into the Value of an Etherised Vaccine in the Prophylactic Treatment of Rabies," MSS Drafts, tables relating to work on rabies, E. 22, JC papers.

129. "An Investigation into the Value of an Etherised Vaccine in the Prophylactic Treatment of Rabies," MSS Drafts, tables relating to work on rabies, table IV, 16–17, E. 22, ibid.

130. H. E. Shortt, R. H. Malone, and A. C. Craighead, "An Investigation into the Relative Immunizing Value of the Kasauli and Paris Strains of Rabies Fixed Virus," *Indian Med. Res. Mem., Supplementary Series to the Indian J. Med. Res.* 28 (1934): 1–78, quotation on 1.

131. Ibid., 2.

132. "Prophylactic Treatment of rabies," *Brit. Med. J.* 1 (June 1933): 979–80.

Table 4 Comparison of the results of treatment with the various vaccines used for class VI cases, 1925–30.

	Carbolized 5%, 1928–30	Carbolized etherized 5%, 1928–30	Alivisatos 5%, 1926–30	Hempt etherized 1.7%, 1926–28	Carbolized 1%, 1926	Carbolized etherized 1%, 1926
Treatment length in days	15	15	15	6	14	14
Condition of virus in vaccine	Dead	Dead	Living	Living	Dead	Dead
Total doses of brain substance in grams	8.5	8.5	8.5	4.0	0.7	1.95
Total number treated	1097	1101	819	723	325	1004
Total deaths	47	72	40	46	28	81
Total mortality rate	**4.28**	**6.54**	**4.88**	**6.36**	**8.62**	**8.07**

Source: E. 22, JC papers (n. 74), 15.

carbolized killed virus of a 5 percent suspension of sheep's brain.[133] Sheep's brain was first used in 1926 by E. C. R. Fox in Calcutta.[134] It was adopted as universal for the Semple vaccine in 1934 as it was cheaper to use particularly when a higher dosage was standardized and mass vaccination was adopted.[135] Decentralization proceeded rapidly, and by 1938 nearly two hundred out centers were supplied with the Kasauli vaccine alone. Similar trends were noticeable in the Madras Presidency too.[136]

The Coonoor figures (Table 5) present the entire history of the evolution of the Semple vaccine. The earliest vaccine used in India was Pasteur's dried cord one, which was replaced in 1911 by the original Semple vaccine (1 percent carbolized rabbit brain). From 1923 this was replaced by the experimental vaccines ranging from 1 percent to 5 percent. From the 1930s the standardized Semple vaccine (5 percent sheep brain, carbolized) was used exclusively. This was also the period when treatment was increasingly decentralized, with more patients treated at the out centers than at Coonoor Pasteur Institute.

Yet at the same time there was evidence that all was not right with the Semple vaccine. As early as 1930 the *BMJ* observed that "[a] few complaints were received about the unfavourable effects of antirabic treatment on the general condition of health."[137] In 1936 S. D. S. Greval (Calcutta School of Tropical Medicine) revisited the almost forgotten question of paralysis from antirabic treatment in India in an article titled "Against Orthodoxies in Rabies" and provided details of cases of paralysis from Semple vaccines.[138] He studied cases of paralysis following "intensive treatment" or administration of higher doses, which as he pointed out was contrary to the "[o]pinion generally held . . . that the incidence of

133. Cunningham, draft of article, "Rabies," E. 25, JC papers.

134. R. Knowles, "Anti-rabic Policy in India," *Indian Med. Gazette* 65 (1930): 155–56, esp. 156.

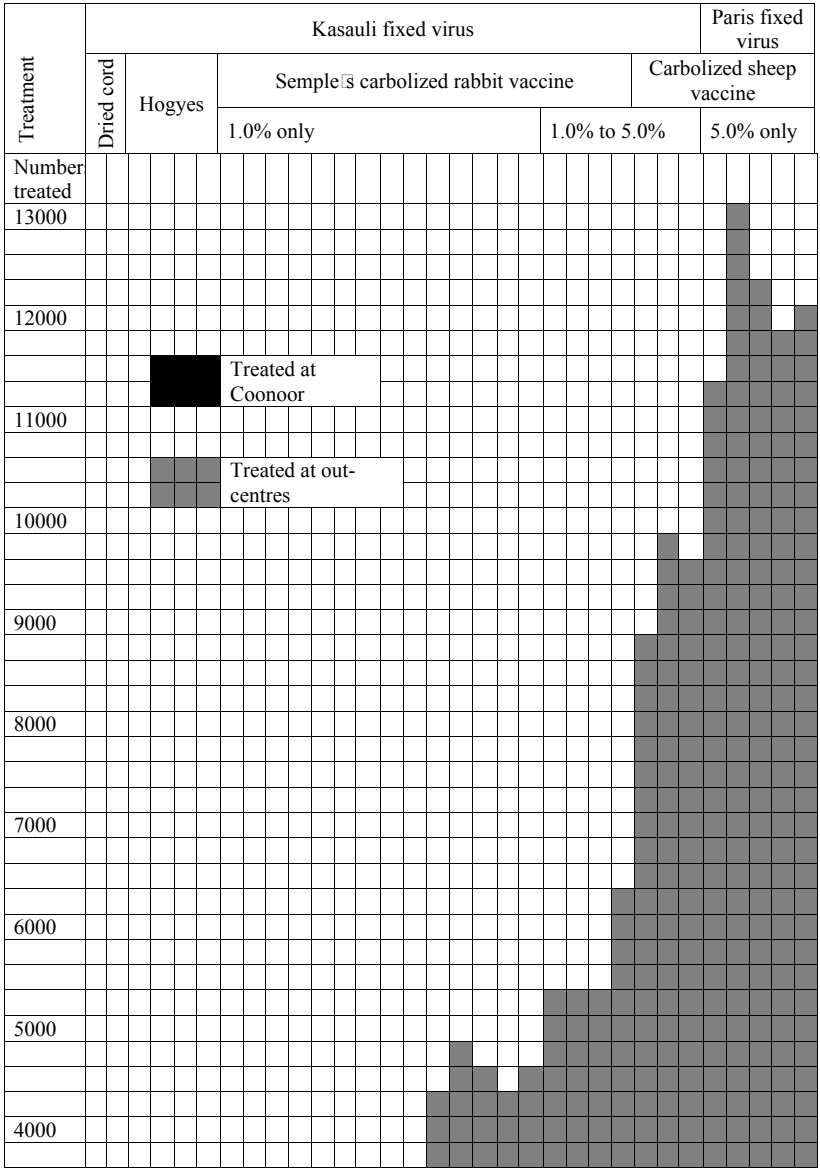
135. Shortt, Malone, and Craighead, "Investigation into the Relative Immunizing Value" (n. 130), 7. Very similar improvements were noticed by Maria J. Otten-van Stockum in Bandung in the Dutch East Indies with her formalized vaccines prepared from monkey brain in 1916. She used monkey brain as it was cheaper and provided more brain matter per animal than the rabbit. Otten-van Stockum, "Rabies Research in the Netherlands Indies," reprinted from "Rabies Researches," in *Meded. Van den Dienst der Volksgezondesd in Nederlandsch Indie* 30 (1941): 269–79.

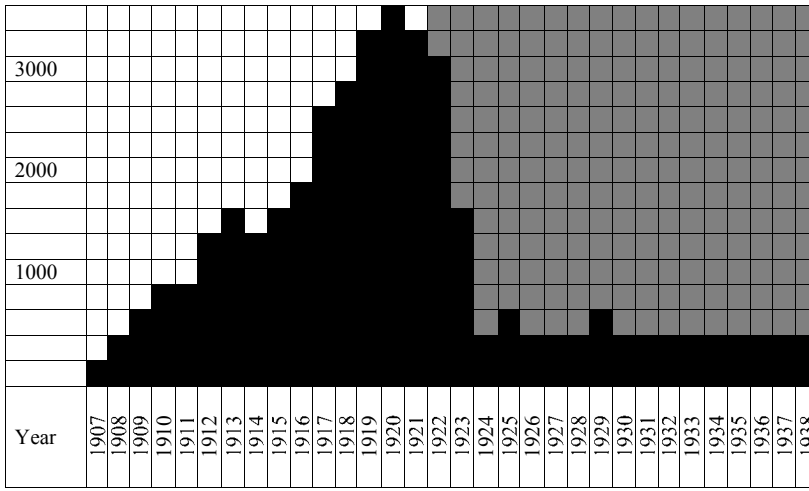
136. *The Pasteur Institute of Southern India, Coonoor, Thirty Eighth Annual Report* (Madras: Pasteur Institute of Southern India, 1940), 15.

137. "Progress of Antirabic Treatment," *Brit. Med. J.* 1 (May 1930): 923–24, quotation on 924.

138. S. D. S. Greval, "Against Orthodoxies in Rabies," *Indian Med. Gazette* 71 (1936): 69–73, 71.

Table 5. Patients treated with antirabies vaccine at the Pasteur Institute, Coonoor, between 1907 and 1938





Source: Pasteur Institute of Southern India (n. 136), 15.

paralysis is independent of the intensity of treatment."[139] He drew the important conclusion that "[c]arbolization of the vaccine does not ward off the sequelæ. It would not be necessary at all to state this point if the opposite were not so widely believed in India by the general medical profession."[140] In the annual reports of the Indian Pasteur Institutes in 1940, it was noted that Semple's vaccine, although effective, was also leading to cases of serious posttreatment paralysis as they contained large quantities of nerve tissues. The reports highlighted the need to produce a vaccine with equal potency but free from such nerve tissues.[141] However, there were few takers for this point of view.

By the 1940s Semple's vaccine was the celebrated one for antirabic treatments all over the world, and as William J. Webster (assistant director of CRI) noted in 1943, "Semple's vaccine is now in general use all over the world and has to a large extent replaced vaccines of the other types."[142]

139. Ibid., 73.

140. Ibid.

141. *Pasteur Institute of Southern India* (n. 136), 17. Also see N. Veeraraghavan, "Phenolized Vaccine Treatment of People Exposed to Rabies in Southern India," *Bull. WHO* 10 (1954): 789–96.

142. Webster, *Rabies and Antirabic Treatment* (n. 41), 7.

[34.230.35.103] Project MUSE (2024-03-28 12:46 GMT)

He reiterated its virtue: "[I]t is a dead vaccine."[143] However, as explained earlier, the actual distinctions between dead and living vaccines remained vague and often indistinguishable.

If clear distinctions between live and dead vaccines were untenable, how do we understand "laboratory rabies" and its links with the live vaccines, an association that was central to the evolution of antirabies vaccines? Here once again, we need to go beyond the phrase of "laboratory rabies" and understand the true nature of the disease.

Deconstructing *Rage du Laboratoire*

As noted earlier, "laboratory rabies" was first identified by scientists opposed to Pasteur's methods as a unique disease produced in the laboratory from Pasteur's vaccines. It was soon adopted by antivivisectionists as a powerful moral and methodological critique of Pasteur's methods. Subsequently it was also adopted by historians like Geison, often with similar moral and medical connotations.[144]

However, the etiology of "laboratory rabies" has remained unclear. The first problem is to identify whether it is a specific disease or a generic term used for several postvaccinal complications and cases of mortality that indicated a different failure of treatment. Often the critiques clumped the various postvaccinal complications under this single label.[145]

Moreover, the nature of the paralytic or neurological complications caused within the laboratory also remained uncertain. Even in the 1930s doubts remained as to the proper etiology of this paralysis. Some held that it was due to the nature of street virus used; others argued that it was due to the nature of the fixed virus. Tinti considered it an anaphylactic phenomenon, while others identified human susceptibility to rabbit brain as the chief factor.[146] The *American Journal of Public Health* confirmed this ambiguity in 1930: "It is now widely believed to be due to the action of some unknown substance contained in the vaccine. We can only accept the statement of the Rabies Conference that our knowledge does not enable us to make positive assertions as to the etiology."[147]

In 1940 McKendrick produced his extensive antirabies vaccination report, which included data from 1,062,707 cases of rabies collected from

143. Ibid.
144. Geison, "Pasteur, Roux, and Rabies" (n. 6), 358.
145. Gelfand, "Day Medicine Changed" (n. 44), 710.
146. "Antirabic Treatment Paralysis," *Amer. J. Pub. Health* 20 (1930): 412–13, esp. 412.
147. Ibid.

Pasteur Institutes all over the world.[148] One important finding was that although he had studied a variety of cases treated by both "live" and "dead" vaccines, in different laboratories and in different conditions, there was no discernible difference in cases of paralysis among patients administered different treatments.[149] This highlighted for the first time the problem in the link between laboratory rabies and live vaccines.[150]

The question is, was "laboratory rabies" an "artificial" or "experimental" form of rabies created in the laboratory as was often supposed, or was it the original affliction that the vaccine had failed to treat, or an entirely different disease, not a form of rabies? By the 1940s, the postvaccinal paralytic cases were defined as a form of encephalitis. In 1949, the International Rabies Committee of the World Health Organization (WHO) focused on the problem of postvicinal paralysis, the "demyelinating lesion" of the cord, and noted that the cases of paralysis were a reaction of some constituent of nervous tissue in the vaccine *rather than an effect of the virus*.[151] It also added that it was a form of encephalomyelitis.[152] Thus, the allergic encephalomyelitis was caused not by the rabies virus, live or dead. It was a condition not necessarily connected to rabies as it could be caused by nonrabid brain matter as well. The agent here was the amount of adult brain tissues, and thus such cases could be caused by dead vaccines as well, particularly in larger doses. Strictly speaking, it was a *different* paralytic disease, not related to rabies. The same year, Charles Pait and Harold Pearson, while studying encephalomyelitis caused by rabies vaccines in Los Angeles, concluded that the most clearly identifiable factors of postvaccinal paralysis (or "vaccine encephalitis") were the indiscriminate vaccine usage and the presence of brain tissue.[153]

Despite these findings, "laboratory rabies" remained a sacrosanct disease, little understood, often feared, but rarely challenged. G. S. Turner (Lister Institute of Preventive Medicine) in 1969 characterized postvaccinal paralytic cases within two categories. While he accepted the new

148. McKendrick, "A Ninth Analytical Review of Reports from Pasteur Institutes on the Results of Antirabies Treatment," *Bull. WHO* 9 (1940–41): 31.

149. Baer, *Natural History of Rabies* (n. 54), 576.

150. Charles F. Pait and Harold E. Pearson, "Rabies Vaccine Encephalomyelitis in Relation to the Incidence of Animal Rabies in Los Angeles," *Amer. J. Pub. Health Nation's Health* 39 (1949): 875–77, esp. 875.

151. "The Treatment of Rabies," *Brit. Med. J.* 2 (October 1950): 823–24, esp. 823.

152. F.–X. Meslin and M. M. Kaplan, "General Considerations in the Production and Use of the Brain Tissue and Purified Chicken-Embryo Rabies Vaccines for Human Use," in *Laboratory Techniques in Rabies*, ed. F.-X. Meslin, M. M. Kaplan, and H. Koprowski (Geneva: World Health Organization, 1996), 223–33, esp. 224.

153. Pait and Pearson, "Rabies Vaccine Encephalomyelitis" (n. 150), 877.

findings the "demyelinating lesions" of the central nervous system caused by brain tissues of mature animals found in dead vaccines, he also insisted that there was another form, which he too referred to as "Laboratory rabies," which was supposedly caused by the living virus.[154] However, he provided no scientific specification of the nature of the disease and its causation. Such demarcations between living and dead vaccines have been constantly revisited and reaffirmed. In 1960 eighteen people died in Fortaleza, Brazil, from postvaccinal paralytic complications. The *Bulletin of WHO* described the deaths following rabies vaccination with Fermi-type vaccine (which, as the report described, was essentially the Semple vaccine, carbolized, 5 percent and from sheep brain) as "*Rage de Laboratoire*" caused by a live vaccine.[155] In 1973, the WHO Expert Committee on Rabies asserted that no vaccines containing a live virus should be employed in human vaccination.[156] While doing so, it did not specify any characteristics of a virus considered as live or dead. Moreover, it did not ban any higher dosage of brain matter or stipulate any limit of dosage, a factor already identified with postvaccinal paralysis in its own 1949 report. Not just for rabies, the WHO in the 1970s was apprehensive about using "live" plague vaccines as well.[157] No clear and consistent definition of what was a living and what was a dead vaccine has ever been produced.

One important and tangible outcome of this was for the Semple vaccine. Once the carbolized vaccine was designated as "dead" and thereby safe, higher dosage of brain matter was sanctioned to be injected in it. The consequence of this increase has been tragic. The Semple vaccine, which until 2001 was the only form of vaccine in the rabies-infected Asian countries like Pakistan, India, and Bangladesh, was provided free of charge by the governments.[158] In 2005 the WHO Committee on Rabies noted that although the use of Semple vaccine was still widespread, it was responsible for severe and long-term side effects. It identified the problem to be in the adult brain matter and initially recommended suckling mouse brain vaccines and later cell culture and purified duck embryo vaccines.[159] This

154. G. S. Turner, "Rabies Vaccines," *Brit. Med. Bull.* 25 (1969): 136–42, esp. 136.

155. Madureira Pará, "An Outbreak of Post-Vaccinal Rabies (*Rage de Laboratoire*) in Fortaleza, Brazil in 1960," *Bull. WHO* 33 (1965): 177–82.

156. *WHO Expert Committee on Rabies: Sixth Report* (WHO technical report series no. 523; Geneva, 1973), 17.

157. Karl F. Meyer, "Effectiveness of Live or Killed Plague Vaccines in Man," *Bull. WHO* 42 (1970): 653–66.

158. *Strategies for the Control and Elimination of Rabies in Asia: Report of a WHO Interregional Consultation* (Geneva: World Health Organization, 2001), 3.

159. *WHO Expert Consultation on Rabies* (WHO technical report series no. 931; Geneva, 2005), first report, 13. The suckling mouse brains were first tried in the 1960s for antirabic

marked a paradigm shift in vaccine research, from the dead/live to the adult/embryonic.

Thus, cases of paralysis were not necessarily linked to live or dead viruses; they were essentially caused by the quantity of adult nerve matter in the vaccines. There was no clear divide between living and dead vaccine, and no real evidence was available that the etherized vaccine was indeed living and carbolized was dead. *Rage du laboratoire*, as it came to be regarded, was essentially a construct that was adopted by the opponents as well as the proponents of Pasteur. In their imagination it became a peculiar form of rabies and was linked to the fear of and fascination with the living virus. It became an important concern for Pasteurists in Europe as it was a powerful weapon in the armory of the anti-Pasteurians. Laboratory rabies and its association with the live vaccine was indeed an exercise (in the Kuhnian sense) in the creation of a regime of problems and solving them.[160]

Conclusion

The history of the Semple vaccine shows the convergence of Pasteurian paradigm and British imperial bacteriology. More importantly, it shows that in these laboratory experiments "living" and "dead" were essentially ideological categories. Yet out of these ideological debates and intangible constructs the Semple vaccine, which became the most popular antirabies vaccine in the world, was produced; millions of patients in Asia, Africa, and the Americas were inoculated with it, many were cured, and several others died from paralytic complications.

These complex, intense, and yet abstract debates about live and dead vaccines highlight the limitation of Bruno Latour's hylozoism. Rather than questioning Pasteur's and other bacteriologists' role in creating the divides between the living and the dead, Latour sought to provide the same life-like agency to the microbes. In doing so, Latour became part of the scientists' world, which was divided by the ideas of the heroic live vaccines and the sterilized dead ones. The viruses themselves, alive or dead, had little agency in it.

In essential terms, the equation was that more nerve tissue produced better mortality rates but also led to more cases of postvaccinal paralysis.

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vaccine. E. Fuenzalida, R. Palacios, and J. M. Borgoño, "Antirabies Antibody Response in Man to Vaccine Made from Infected Suckling-Mouse Brains," *Bull. WHO* 30 (1964): 431–36.

160. Thomas S. Kuhn, "The Essential Tension: Tradition and Innovation in Scientific Research," in *The Philosophy of Science*, ed. Richard Boyd, Philip Gasper, and J. D. Trout (Cambridge, Mass: MIT Press, 1991), 139–58.

This was not due to the nature of the vaccine, live or dead. Cunningham was right to point out the dangers of the carbolized vaccine, which could lead to increased use of nerve cells. His gradation method of vaccination according to the severity of cases was also innovative. However, he too was caught up in the Pasteurian paradigm of live germs.

Why did such a divide endure for so long and so forcefully? The debates around the living and dead were important because they referred to the two most important concerns of vaccine research, potency and safety. Dead vaccines were identified as safe, stable, and dependable. It was also because vaccine research is result oriented, and one way to resolve some of the complex problems faced by antirabic vaccination in terms of safety and mortality was by creating clear demarcations and identities of diseases and their vaccines. These were at the core of the modern understanding of "virus," organically linked to ideas of "virulence." From Pasteur's time scientists had engaged with the virulence of viruses to produce potent antivirus, the fear and fascination with the living and the virulent in a world of germs.

Finally, there were ambiguities in the understanding of the living and the dead itself in contemporary scientific thinking, an ambiguity that few scientists confronted or referred to. A rare and wonderful exposition of this came in 1928, from the pathologist and naturalist Arthur E. Boycott in his presidential address to the Royal College of Medicine, where he spoke about "The Transition from Live to Dead." He elaborated how in nature a polarization between the living and the dead was false. The two were in a continuum,

> [in] an assemblage of concurring and converging probabilities which encourage one to think it possible that things which are alive and things which are not alive constitute in effect one series, beginning with hydrogen atoms and reaching up to man, and perhaps to angels, not arranged in a continuous linear succession but on a scheme resembling the phylogenetic line of the animal kingdom. . . . Such a view satisfies our natural antipathy to a dualistic explanation of the universe and makes the old controversy about vitalism and mechanism largely unnecessary. It tells us nothing about the nature of life; by indicating that organisms are analogous to elements, it encourages us to think of life as being as insoluble as gravitation. . . . If you like to be paradoxical, you can say that live things are dead, or if you prefer it, that dead things are alive. Both at bottom have much the same characters, and it is unlikely that any sharp distinctions between them can be drawn.[161]

161. Arthur E. Boycott, "The Transition from Live to Dead: The Nature of Filterable Viruses," *Proc. Roy. Soc. Med.* 22 (1928): 55–69, quotation on 60.

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