
The World's First Immunization Campaign: The Spanish Smallpox Vaccine Expedition, 1803–1813

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SUMMARY: Smallpox produced the death of up to thirty percent of those infected, so Jenner's preventive method spread quickly. The Spanish government designed and supported a ten-year effort to carry smallpox vaccine to its American and Asian territories in a chain of arm-to-arm vaccination of children. An expedition directed by Doctor Francisco Xavier de Balmis sailed from Corunna in November 1803, stopping in the Canary Islands, Puerto Rico, and Venezuela. Balmis led a subexpedition to Cuba, Mexico, and the Philippines; his assistants returned to Mexico in 1807, while Balmis took vaccine to China and returned to Spain (and again to Mexico, 1810–13). Vice-director José Salvany and his staff took vaccine to present-day Colombia, Ecuador, Peru, Bolivia, and Chilean Patagonia. The Spanish Royal Philanthropic Vaccine Expedition shows the first attempts to solve questions still important for the introduction of new immunizations—professionalization in public health, technology transfer, protection of research subjects, and evaluation of vaccine efficacy, safety, and cost.

KEYWORDS: smallpox, vaccination, Balmis-Salvany expedition, Spanish America, public health, technology transfer

The Royal Philanthropic Vaccine Expedition, a ten-year effort of global dimensions, carried smallpox vaccine from Spain to the Caribbean, to New Spain (Mexico) and Guatemala, to Venezuela, down the length of the Pacific coast of South America and up to its Andean provinces, to the Philippines, and to China. The achievements of the small group of adult participants and the children in whose arms vaccine was transported have been described in numerous historical publications, but the expedition's

We are grateful to the Balmis scholars who have generously shared with us their unpublished materials and notes, especially Thomas B. Colvin, Susana M. Ramírez, Michael M. Smith, and C. Michele Thompson. We thank also Professor Carmen M. Santos-Corrada at the Conrado Asenjo Library, Medical Sciences Campus, University of Puerto Rico.

organization, goals, methods, and accomplishments have failed to attract attention and study as a precedent for modern vaccination campaigns.

Current immunization programs must pursue high coverage of a clearly defined target population, manage a reliable logistics and transport system, employ trained health workers, reduce administrative and geographical barriers (with fixed and, if necessary, mobile delivery sites), and inform and motivate the population to make use of the vaccine.¹ Some of the major lessons learned by the Expanded Programme on Immunization of the World Health Organization in the 1980s also include the following: personal involvement of political, religious, and social leadership mobilizes communities; communication is a critical component of a program and uses multiple channels (face-to-face, print, mass media) to deliver the message; staff training provides the technical skills for planning and management; successful programs have a process measure (coverage) as well as outcome indicator (disease incidence); disease surveillance helps focus efforts on areas of greatest risk; decentralization of resources, coupled with a national plan of action, permits more effective and rapid activities; research and development provide a technical basis for advancing program goals; unbalanced concerns over risks, and public apathy toward immunization, as disease incidence declines, must be countered everywhere.² As we will explain, the organizers and staff of the Spanish vaccine expedition were aware of the importance of many of these concepts even at the planning of their voyage. Although their solutions to these problems proceeded from the knowledge and attitudes of their time, their foresight for the requirements of success in the field marks them as precursors of modern vaccination campaigns.

We present a summary of the Royal Philanthropic Vaccine Expedition's progress, based on standard extensive secondary accounts, recently reported data (almost entirely unavailable in English), and our own archival research. We reframe the conventional analysis of the expedition in the context of the demands of the situation, an international vaccination campaign, which were unique at the time. We then briefly examine the expedition's goals and development in comparison to the only contemporary governmentally structured vaccination effort, in British India. The Spanish expedition was the first campaign to identify and anticipate solutions for problems that were then without precedent but that would recur in many vaccination programs thereafter. Stated in modern terms,

1. Felicity T. Cutts and Jean-Marc Olivé, "Vaccination Programs in Developing Countries," in *Vaccines*, ed. Stanley A. Plotkin and Walter A. Orenstein (Philadelphia: W. B. Saunders, 1999), pp. 1047–73, esp. 1050.

2. Paul F. Basch, *Vaccines and World Health: Science, Policy, and Practice* (New York: Oxford University Press, 1994), pp. 174.

these issues are clinical (regarding vaccine quality and safety), administrative (funding, centralization, specialization of staff, institutionalization), epidemiologic (broad coverage, disease surveillance), and ethical (protection of vaccinees, consent to treatment).

The Public Health Problem

At the close of the eighteenth century, the threat of smallpox had a different meaning for Spain than it did for most of her neighbors. Morbidity and mortality rates at home, although severe, were similar to those in other European countries, where smallpox could result in the death of up to one third of cases. In Spain's extensive overseas territories, the impact of successive epidemics was devastating. As the disease was introduced in the Americas around 1518, the native peoples had no genetic resistance to the virus or ancient empiric treatment or preventive methods. Case-fatality rates could exceed fifty percent.³ The contagiousness of the disease was well recognized, but strict case isolation was rarely enforceable.

Inoculation (variolation), which had been practiced in Asia and Africa since ancient times, was introduced to the Western Hemisphere through its use in London and Boston during epidemics in 1721. Violent medical disputes raged for the next eighty years on its risks and benefits. Inoculation was performed by introducing a small amount of liquid from a smallpox vesicle into the subcutaneous tissue of a healthy subject, who then acquired a mild case of smallpox, which usually healed without scarring.⁴ While mortality for smallpox acquired by natural infection was fifteen to thirty-three percent, the mortality rate for inoculation in the late eighteenth century was less than one fifth of a percent, one to two hundred times less.⁵ The method was not innocuous, however. Critics of inoculation argued that it contributed to the spread rather than to the prevention of smallpox; its protective efficacy was uncertain and depended on the specific method used. It exposed the individual to some risk of injury (blindness, disfigurement) or even death, when it was possible that the person would never contract natural smallpox.⁶ In Spain, variolation was used

3. Frank Fenner, Donald A. Henderson, Isao Arita, Zdeno Jezek, and Ivan D. Ladnyi, *Smallpox and its Eradication* (Geneva: World Health Organization, 1988), pp. 236–38.

4. Arnold C. Klebs, "The Historic Evolution of Variolation," *Bull. Johns Hopkins Hosp.*, 1913, 24: 69–83.

5. Peter Razzell, *The Conquest of Smallpox: The Impact of Inoculation on Smallpox Mortality in Eighteenth Century Britain* (Firle, Sussex: Caliban Books, 1977), pp. 133, 23.

6. Francisco Gil, *Disertación físico-médica en la qual se prescribe un método seguro para preservar a los pueblos de viruelas hasta lograr la completa extinción de ellas en todo el reyno* (Madrid, 1784), pp. 29–30, 37–40, 76–78.

in 1728 but was rarely practiced until the 1770s.⁷ Although never really popular in Spain, it was used sporadically in some American territories, mostly at the time of an epidemic: Santiago de Chile in 1765; Caracas in 1766; Lima in 1777 and 1797; México in 1779 and 1797; Guatemala in 1780 and 1794; Bogotá and environs in 1756–57, 1782, and 1796; Puerto Rico in 1792; and Paraguay in 1797.⁸

An abridged version of Edward Jenner's 1798 *Inquiry* into the use of cowpox as a preventive measure against smallpox appeared early in 1799 in Spain's *Semanario de Agricultura y Artes*. Jenner's method was safer and easier to use than variolation and could offer protection to large segments of the population. The vaccine reached Spain in December 1800, and by the end of 1801, several thousand vaccinations had been reported in Catalonia, Madrid, Navarre, and the Basque Country.⁹ From 1799 to 1804, dozens of translations and original reports, treatises, and bulletins, as well as newspaper articles and editorials on smallpox vaccination were published in Spain. These documents circulated widely and were also read carefully in Spanish America.¹⁰

Proposals for a Solution

Attempts were made in many territories to obtain the vaccine lymph dried onto silk threads or sealed between glass plates, but such conservation methods proved unreliable on lengthy journeys and in warm climates. Although transporting the vaccine from Europe was an expensive undertaking whose success was uncertain, King Carlos IV of Spain instructed the Council of the Indies in March 1803 to evaluate the means with which it could introduce vaccine in the American and Asian possessions.¹¹ It

7. Luis S. Granjel, *Historia de la medicina española* (Barcelona: Sayma, 1962), p. 115.

8. Francisco Guerra, *Epidemiología americana y filipina, 1492–1898* (Madrid: Ministerio de Sanidad y Consumo, 1999), pp. 379, 389, 393, 396, 408, 414, 419, 424, 429. For Bogotá, see also Marcelo Frías Núñez, *Enfermedad y sociedad en la crisis colonial del Antiguo Régimen (Nueva Granada en el tránsito del siglo XVIII al XIX: las epidemias de viruelas)* (Madrid: Consejo Superior de Investigaciones Científicas, 1992), pp. 66–68; for Chile and Peru, see Juan B. Lastres, *La salud pública y la prevención de la viruela en el Perú* (Lima: Ministerio de Hacienda y Comercio, 1957), pp. 39–45.

9. Antonio Rumeu de Armas, "Primeros progresos de la vacunación en España," *Medicina Española*, 1940, 4: 317–29.

10. José G. Rigau-Pérez, "La difusión en Hispanoamérica de las primeras publicaciones españolas sobre vacuna, 1799–1804," *Asclepio*, 1992, 1: 165–79; Guillermo Olagüe de Ros and Mikel Astrain Gallart, "Propaganda y filantropismo: los primeros textos sobre la vacunación jennariana en España (1799–1801)," *Medicina e Historia* (Tercera época), 1995, 56: 1–16.

11. The first published report on the Spanish Philanthropic Vaccine Expedition appeared as a supplement (*Una relación de la Expedición de Balmis a América*) to the *Gazeta de Madrid* on

would seem incredible that the Spanish government, with the economic and political problems it suffered in 1803 and the slow communications of the times, could successfully distribute vaccine throughout the world, but it had developed great expertise in the organization of transatlantic expeditions in recent decades, focused mainly on the exploration of the geography and natural resources of the Indies.¹² Two centuries before “globalization,” the Spanish government established credit lines and paid expenses and salaries simultaneously in Spain (to relatives of expedition staff) and wherever its agents fulfilled their missions. In the case of the vaccine expedition, there were even requests for proposals and evaluations by experts who then modified the initial plans for projects, but we cannot yet speak of equal opportunities or impartiality in the evaluations.

The government’s departments (“secretariats”) were five: State, Finances, Navy, War, and Gracia y Justicia, or Beneficence and Justice. The latter’s jurisdiction included sanitary affairs, and among the many bodies over which it exercised oversight was the Board of King’s Surgeons (Junta de Cirujanos de Cámara del Rey). The Council of the Indies, on its

14 October 1806, shortly after Balmis’s return to Spain and reception at court. For nearly eighty years thereafter, most descriptions of the expedition summarized this account. Following Eduardo Moreno Caballero’s original research published as *Sesión apologetica dedicada al Dr. D. Francisco Xavier de Balmis Berenguer* (Valencia: Ferrer de Orga, 1885), a body of literature began to develop founded on analysis of archival documents; see Emili Balaguer i Perigüell, “La historiografía científicomédica sobre Balmis y la Real Expedición Filantrópica de la Vacuna,” in *La Real Expedición Filantrópica de la Vacuna: doscientos años de lucha contra la viruela*, ed. Susana Ramírez, Luis Valenciano, Rafael Nájera, and Luis Enjuanes (Madrid: Consejo Superior de Investigaciones Científicas, 2004), pp. 41–60. One of the early studies based on comprehensive documentary review (1948) was by Gonzalo Díaz de Yraola, *La vuelta al mundo de la Expedición de la Vacuna (1803–1810)* [*The Spanish Royal Philanthropic Expedition: The Round-the-World Voyage of the Smallpox Vaccine (1803–1810)*], 2nd ed., facsimile with translation to English, trans. and ed. Catherine Mark (Madrid: Consejo Superior de Investigaciones Científicas, 2003). To avoid individual footnotes documenting each incident in the expedition, we refer the reader to this publication for details. Although it is not the most recent account, it has a chronological organization, an appendix summarizing the course of the expedition, and an index of names, dates, and places that facilitates location of specific items. We provide other references for additions, corrections, and clarifications resulting from later research.

12. Francisco Javier Puerto Sarmiento, *Ciencia de cámara. Casimiro Gómez Ortega (1741–1818), el científico cortesano* (Madrid: Consejo Superior de Investigaciones Científicas, 1992); Alejandro R. Díez Torre, Tomás Mallo, Daniel Pacheco Fernández, and Ángeles Alonso Flecha, coords., *La ciencia española en ultramar. Actas de las I Jornadas sobre España y las expediciones científicas en América y Filipinas* (Aranjuez: Doce Calles, 1991); Alejandro R. Díez Torre, Tomás Mallo, and Daniel Pacheco Fernández (coords.), *De la ciencia ilustrada a la ciencia Romántica. Actas de las II Jornadas sobre España y las expediciones científicas en América y Filipinas* (Aranjuez: Doce Calles, 1995).

part, responded to the king through the secretaries (department heads). The council received information and petitions from the authorities in the Indies and could, on its decision, demand reports.¹³

The council responded to the king's order with a plan it had already requested from Dr. José Flores, a Guatemalan expert on smallpox inoculation, physician of the royal chamber, and resident of Madrid. On 28 February 1803, he proposed two expeditions, one to the Caribbean, Mexico, and Central America and another to South America.¹⁴ The council suggested that Flores and Francisco Xavier de Balmis be asked to lead the expeditions. The plans evolved through consultations among the Council of the Indies, the Secretary of Beneficence and Justice, and the Board of King's Surgeons.¹⁵ Balmis was soon selected to head the expedition. At forty-nine years of age, he had served as a military surgeon in several campaigns and in hospitals on both sides of the Atlantic. He had ample medical experience in the Americas, was an ardent promoter of Jenner's discovery, had acted as a vaccinator in Madrid, and had recently translated Moreau de la Sarthe's 1801 treatise on vaccination technique.¹⁶ Balmis proposed a route to the Caribbean territories and to Mexico, followed by a sea journey to Lima, overland expeditions branching to Quito, Chile, and Buenos Aires, and a later voyage to the Philippine Islands. His systematic plan detailed the expedition's logistics and specified the duties of the medical and nursing staff. Its essence lay in three objectives: cost-free vaccination of the general population, training of local physicians in correct vaccine administration, and establishment of central and regional vaccination boards (*Juntas de Vacunación*) to preserve and distribute the vaccine and to maintain orderly immunization records for further investigation.¹⁷

Carlos IV approved the project in June 1803, with Balmis as its director; the royal treasury would assume the cost of the undertaking. The authorities in Spain's American and Asian possessions received orders to provide

13. José Antonio Escudero, *Los cambios ministeriales a finales del antiguo régimen* (Seville: Universidad de Sevilla, Tusquets, 1975), pp. 9, 35–37.

14. Rodolfo MacDonal Kanter, "Segundo centenario de la llegada de la vacuna contra la viruela en el Reino de Guatemala, 1804–2004," *Anales de la Academia de Geografía e Historia de Guatemala*, 2004, LXXIX: 183–210, esp. pp. 196–97.

15. Michael M. Smith, "The 'Real Expedición Marítima de la Vacuna' in New Spain and Guatemala," *Trans. Am. Philos. Soc.*, 1974, 64: 1–74, esp. pp. 13–15.

16. Jacques-Louis Moreau de la Sarthe, *Traité Historique et Pratique de la Vaccine* (Paris: Bernard, 1801). For a facsimile reprint of the translation, see Francisco Javier Balmis, *Prólogo y traducción castellana del "Tratado histórico y práctico de la vacuna," de J. L. Moreau (1803)*. Introductory study by Emili Balaguer i Perigüell (Valencia: Edicions Alfons el Magnànim, 1987).

17. Smith, "Real Expedición" (n. 15), pp. 15–16.

logistic support and underwrite local expenses, to inform the population of the benefits of the vaccine, and to encourage vaccination. The expedition staff was named, and ultimately included two physician-surgeons (Manuel Grajales and Antonino Gutiérrez), two surgeons (José Salvany and Rafael Lozano), one practitioner (Francisco Pastor) and four nurses (Basilio Bolaños, Ángel Crespo, Pedro Ortega, and Antonio Pastor; see Table 1). Salvany was appointed vice-director of the expedition. To transport the live vaccine on the two-month voyage to the New World, twenty-two nonimmune orphaned boys, ages three to nine years old, would be vaccinated during the crossing by serial arm-to-arm inoculation. These children, and many others who would succeed them, would be under the care of Isabel Zendala y Gómez, rectora of the Corunna Foundling Home and the only woman to participate in the expedition.¹⁸

The Royal Philanthropic Vaccine Expedition

The expedition finally sailed from Corunna aboard the 160-ton corvette *María Pita* on 30 November 1803 (Figure 1). A stopover in the Canary Islands resulted in a jubilant reception, the first vaccinations in the archipelago, and the creation of a vaccination board. After a stormy ocean voyage, the expedition reached Puerto Rico in February 1804.¹⁹ Balmis was disconcerted to find that the vaccine had been introduced shortly before their arrival, brought from the neighboring Danish island of St. Thomas at the request of San Juan physician Francisco Oller to combat a smallpox outbreak. The combination of Balmis's exacting inquiries into the efficacy of the program Oller had initiated and his ill-concealed resentment led to confrontations with local authorities. The cost of maintaining the unexpectedly large group was another local concern. When the merit

18. We do not have a consistent name (or spelling) for the rectora; for the variants and their origins, see Susana M. Ramírez-Martín and José Tuells, "Doña Isabel, la enfermera de la Real Expedición Filantrópica de la Vacuna," *Vacunas*, 2007, 8: 160–66. Most documents refer to her by her title, "la Rectora," and none with her signature has been found. We have chosen to call her Zendala y Gómez on the basis of documents signed by the people who knew her. The manifest of members of the expedition on arrival in Manila, 15 April 1805, signed by Balmis and sent to Spain twice in copies signed by different persons, both times identified her as Isabel Zendala y Gómez: Archivo General de Indias de Sevilla, Indiferente General, Legajo 1558A (henceforth AGI, IG 1558A). Antonino Gutiérrez, in his petition in Mexico, 8 January 1812, also calls her Isabel Cendala y Gómez: Archivo General de la Nación, Mexico, Epidemias, vol. 17: 293.

19. Archivo General de Puerto Rico, San Juan, Puerto Rico, Spanish Governors, Box 146, Legajo 1379, Francisco Xavier de Balmis to José Antonio Caballero, San Juan, 27 February 1804.

Table 1. Staff of the Royal Philanthropic Vaccine Expedition: Summary of Personal and Professional Data

Name	Training in Spain	Position in the expedition	Birth	Marital status on departure	Death or last reported whereabouts	Areas of principal activity
Balmis y Berenguer, Francisco Xavier de	Physician and surgeon (Doctor in Medicine)	Director	Alicante, 2 December 1753	Widowed at death ^a	Died in Madrid 12 February 1819	In charge from Corunna around the world (1803–6). Returned to Mexico (1810); back in Spain in 1813.
Salvany Lieopart, José	Surgeon	Vice-director	Barcelona, 19 January 1774 ^b		Died in Cochabamba, Bolivia 21 July 1810	In charge from La Guayra (1804) to Cochabamba (1810).
Grajales Gil de la Serma, Manuel Julián	Physician and surgeon	Salvany's First Assistant	Sonseca (Toledo), 15 January 1775 ^c	Single; married later in Peru; ^d	Captured by insurgents in 1813, served as army surgeon in Chile until 1824, then returned to Spain and served as military surgeon until 1847. ^e	Alone or with Lozano or Bolaños, on multiple regional expeditions in present-day Colombia, Ecuador, and Peru (1804–7). With Bolaños, worked independently from Salvany, from Lima (1807) to Chiloé, in Patagonia (January 1812).

1855^f

Table 1 (*continued*). Staff of the Royal Philanthropic Vaccine Expedition: Summary of Personal and Professional Data

Lozano Pérez, Rafael	Surgeon	Salvany's Second Assistant	Province of Cuzco, 1809 ^s	Alone or with Grajales, on multiple regional expeditions in present-day Colombia, Ecuador, and Peru (1804–7). Alone in the Peruvian highlands (1807–9).
Bolaños, Basilio ^h	Nurse		Married	Buenos Aires, 1809; With Grajales, on multiple regional expeditions in present-day Colombia, Ecuador, and Peru (1804–7). With Grajales, worked independently from Salvany, from Lima (1807) to Chiloe, in Patagonia (January 1812).
Gutiérrez Robledo (or López de Robredo), Antonino	Physician and surgeon	Balmis's Assistant	Madrid, 10 May 1773 ⁱ	Died in Mexico City, 1850 ^s
				Campeche (July 1804) and Central Mexico (November 1804–January 1805). ^k Led the group in the Philippines and back to Mexico (August 1805–August 1807).

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Table 1 (*continued*). Staff of the Royal Philanthropic Vaccine Expedition: Summary of Personal and Professional Data

Name	Training in Spain	Position in the expedition	Birth	Marital status on departure	Death or last reported whereabouts	Areas of principal activity
Pastor Balmis, Francisco	Practitioner	(Balmis's nephew)			To Spain in late 1810	Mérida to Guatemala City (July 1804–January 1805). With Ortega, to the southern Philippines (September 1805–June 1806). ¹
Pastor Balmis, Antonio	Nurse	(Balmis's nephew)			To Spain in late 1810, alive in 1824 ^m	New Spain and the Philippines
Ortega, Pedro ^a	Nurse			Married, two children	Died in Manila, before June 1806	With F. Pastor, to the southern Philippines (September 1805–Spring 1806) ^o
Crespo, Ángel ^b	Nurse	Secretary, nurse after May 1804			Died in Mexico City, 1850s ^d	New Spain and the Philippines
Zendala y Gómez /Sendales /Gómez Sandalla /Cendales y López, Isabel	Rectress of the Corunna Foundling Home	(maternal attentions to children)		Single, with adopted founding (Benito Vélez)	1808; 1811 ^r	New Spain and the Philippines

- ^aArchivo Histórico de Protocolos, Madrid, No. 22326, Will of Francisco Xavier de Balmis, f. 212.
- ^bAlejandro Belaustegui Fernández, *José Salvany y otros médicos militares ejemplares* (Madrid: Imprenta Ministerio de Defensa, 2006), p. 19.
- ^cSusana M. Ramírez Martín, *La mayor hazaña médica de la colonia. La Real Expedición Filantrópica de la Vacuna en la Real Audiencia de Quito* (Quito, Ecuador: Ediciones Abya-Yala, 1999), p. 265.
- ^dArchivo Histórico de Protocolos, Madrid, Nos. 23522, 24939: Wills of Manuel Julián Grajales and his wife Josefa Uztariz Bosquets, 1832 and 1844.
- ^eRamírez Martín, *La mayor hazaña* (n. c), p. 269; Julio del Castillo y Domper, *Real Expedición Filantrópica para propagar la vacuna en América y Asia* (Madrid: Imp. Ricardo F. de Rojas, 1912), p. 151.
- ^fEnrique Laval Manríquez, "La viruela en Chile," *Anales Chilenos de Historia de la Medicina*, 1967–1968; 9–10: 203–76, esp. 276.
- ^gArchivo General de Indias de Sevilla, Indiferente General, Legajo 1558A (hereafter *AGI*, IG 1558A), Salvany to Junta Suprema, La Paz, 30 March 1809.
- ^hMarital status, in Buenos Aires 1809 in *AGI*, IG 1558A, extract note quoting Balmis, 24 February 1809; in Chile see Laval Manríquez, "La viruela en Chile," (n. f), p. 262.
- ⁱRamírez Martín, *La mayor hazaña* (n. c), p. 271.
- ^jMichael M. Smith, "The 'Real Expedición Marítima de la Vacuna' in New Spain and Guatemala," *Trans. Am. Philos. Soc.*, 1974, 64: 1–74, p. 68.
- ^k*Ibid.*, pp. 31, 44–47, 54.
- ^l*Ibid.*, p. 58; Ramírez Martín, *La mayor hazaña* (n. c), pp. 153–55.
- ^mBoth Pastor brothers to Spain: Smith, "The 'Real Expedición'" (n. j), pp. 65, 68; *AGI*, IG 1558A, extract note indicating copy of document provided by request of Antonio Pastor y Balmis, 1 July 1824; Archivo General de la Nación, México, Epidemias, vol. 17: 276–277v. Francisco Xavier de Balmis to Antonino Gutiérrez, 28 November 1806.
- ⁿSmith, "The 'Real Expedición'" (n. j), pp. 64–65.
- ^o*Ibid.*, p. 58; Ramírez Martín, *La mayor hazaña* (n. c), pp. 153–55.
- ^pSmith, "The 'Real Expedición'" (n. j), pp. 48, 68.
- ^q*Ibid.*, p. 68.
- ^r*Ibid.*, pp. 65, 67.

of Oller's method was confirmed, Balmis sailed in March for Venezuela without having established a complete vaccination program.²⁰

Caracas embraced the expedition with crowds and carriage processions, festivities and fireworks, music, theater, and a thanksgiving Mass. Due to the enthusiastic collaboration of the civil and ecclesiastic authorities, the course of activities in Venezuela matched Balmis's expectations, with mass vaccinations (more than 12,000 in less than a month), training of local physicians, vaccine distribution in cities and outlying regions, and the creation of the first central vaccination board, on which all others in Spanish America would be modeled.²¹

Given the enormity of the enterprise and the vast area it would encompass, Balmis decided to divide the group at this time. With Gutiérrez, Antonio and Francisco Pastor, Ortega, Crespo, Zendala, the boys brought from Spain, and fresh recruits from Venezuela, Balmis would take the vaccine to the viceroyalty of New Spain, whereas Salvany would proceed to the viceroyalties of New Granada, Peru, and Rio de la Plata, accompanied by Grajales, Lozano, Bolaños, and four Venezuelan boys serving as the first carriers in the chain. The two expeditions were independent thereafter; most likely, none of their respective members met again. After their separation, both groups would deviate frequently from the original plan, with local politics, smallpox outbreaks, and geography dictating operational structures, pace, and routes. Two staff members died on duty (Ortega and Salvany; see Table 1). Balmis, his nephews (the Pastors), and, much later, Grajales, returned to Spain, but Gutiérrez and Crespo stayed in Mexico. We do not know the final whereabouts of three staff members: Lozano, Bolaños, and Isabel Zendala. The foundlings from Galicia were entrusted to the Real Hospicio de Pobres in Mexico City, and most were adopted by teachers and merchants.²²

The Balmis Subexpedition

When Balmis and his staff disembarked in Cuba in May 1804, they knew that the vaccine had again preceded them (Fig. 2, Table 2).²³ The cour-

20. José G. Rigau-Pérez, "The Introduction of Smallpox Vaccine in 1803 and the Adoption of Immunization as a Government Function in Puerto Rico," *Hispanic Am. Hist. Rev.* 1989, 69: 393–423.

21. José Esparza and Germán Yépez Colmenares, "Viruela en la Venezuela colonial: epidemias, variolización y vacunación," in Ramírez et al. (n. 11) *La Real Expedición Filantrópica de la Vacuna*, pp. 89–119.

22. Smith, "Real Expedición" (n. 15), p. 34.

23. A Havana newspaper with the news reached Puerto Rico before Balmis's departure for Venezuela; see Rigau-Pérez, "The Introduction of Smallpox Vaccine" (n. 20), p. 412.

Table 2. Chronology of First Successful Smallpox Vaccinations, by Geographic Area

Place (modern designation)	Source	Smallpox vaccination introduced		Spanish Vaccine Expedition dates (1803–12)
		Date	Procured (or first used) by	
Balmis subexpedition				
Canary Islands	Expedition	December 1803	Balmis	9 December 1803–6 January 1804 ^a
Puerto Rico	St. Thomas (Danish Virgin Island)	November 1803	Oller	9 February–12 March 1804 ^b
Venezuela	Expedition	March 1804	Balmis	20 March–8 May 1804 ^c
Cuba	Puerto Rico	February 1804	Romay	26 May–18 June 1804 ^d
Mexico	Cuba	April 1804	Arboleaya (Pérez Carrillo)	25 June 1804–8 February 1805 ^e
Guatemala	Veracruz (from Cuba)	May 1804	Pavón (Esparragosa)	Late 1804 ^f
Philippine Islands	Expedition	April 1805	Balmis	15 April–3 September 1805 (Balmis) 15 April 1805–mid-April 1807 (others) ^g
Macao	Philippines ^h	May 1805	Huet	16 September–5 October 1805 December 1805–February 1806 ⁱ

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Canton (Guangzhou, China)	Macao (from the Philippines) ^j	mid-1805	Pearson	October–December 1805 ^k
St. Helena	Expedition ^l	June 1806	Balmis	?–17 June 1806 ^m
Salvany subexpedition				
Colombia	Expedition ⁿ	May 1804	Salvany	13 May 1804 (Magdalena River) 18 December 1804 (Santa Fe de Bogotá)
Ecuador	Expedition	May 1805	Salvany	27 May 1805 (Popayán) 16 July 1805 (Quito) ^o
Peru	Buenos Aires, overland	October 1805	(Belomo, in Lima) ^p	23 December 1805 (Piura) 23 May 1806 (Lima) 15 September 1807 (Arequipa) 20 September 1808 (Puno)
Bolivia	Lima	February 1806	Haenke	Early 1809 (La Paz)—21 July 1810 ^q
Chile	Buenos Aires, by sea	October 1805	(Chaparro, in Santiago)	18–19 December 1807 (Grajales arrived in Valparaíso)—January 1812 (departed for Lima) ^r

Continued on p. 78

Table 2 (*continued*). Chronology of First Successful Smallpox Vaccinations, by Geographic Area

- ^aVíctor García Nieto and Justo Hernández, "La Real Expedición Filantrópica de la Vacuna en Canarias (9 de diciembre de 1803–6 de enero de 1804)," *Asclepio*, 2005, 57: 151–71.
- ^bSusana M. Ramírez Martín, *La mayor hazaña médica de la colonia. La Real Expedición Filantrópica de la Vacuna en la Real Audiencia de Quito* (Quito, Ecuador: Ediciones Abya-Yala, 1999), pp. 305, 341.
- ^c*Ibid.*, pp. 344, 350.
- ^d*Ibid.*, p. 307.
- ^eGonzalo Díaz de Yraola, *La vuelta al mundo de la Expedición de la Vacuna (1803–1810)* [*The Spanish Royal Philanthropic Expedition: The Round-the-World Voyage of the Smallpox Vaccine (1803–1810)*], 2nd ed., facsimile with translation to English, trans. and ed. Catherine Mark (Madrid: Consejo Superior de Investigaciones Científicas, 2003), p. 51; Michael M. Smith, "The 'Real Expedición Marítima de la Vacuna' in New Spain and Guatemala," *Trans. Am. Philos. Soc.*, 1974, 64: 1–74, pp. 23–24; Ramírez Martín, *La mayor hazaña* (n. b.), pp. 356, 368.
- ^fSmith, "The 'Real Expedición'" (n. e), pp. 51–52, 54–55; Rodolfo MacDonald Kanter, "Segundo centenario de la llegada de la vacuna contra la viruela en el Reino de Guatemala, 1804–2004," *Anales de la Academia de Geografía e Historia de Guatemala*, 2004, LXXIX: 183–210, p. 202.
- ^gThomas B. Colvin, "Arms Around the World: The Introduction of Smallpox Vaccine Into the Philippines and Macao in 1805," *Revista de Cultura*, 2006, 18, 70–88, pp. 81, 85.
- ^hShortly after Balmis's arrival in Manila, Pedro Huet carried vaccine from Manila to Macao (May 1805). On his arrival in the following September, Balmis reintroduced the vaccine, as it had been lost. Ramírez Martín, *La mayor hazaña* (n. b.), p. 326; Isabel Morais, "Smallpox Vaccinations and the Portuguese in Macao," *Review of Culture*, 2006, 18: 113–24, p. 118.
- ⁱRamírez Martín, *La mayor hazaña* (n. b.), pp. 371–73.
- ^jDr. Alexander Pearson briefly introduced the vaccine from Macao in mid-1805. We don't know the extent of his activities, except that vaccine was extinguished soon thereafter and reintroduced with Balmis's arrival. John Z. Bowers, "The Odyssey of Smallpox Vaccination," *Bull. Hist. Med.*, 1981, 55: 17–33, p. 33.
- ^kRamírez Martín, *La mayor hazaña* (n. b.), pp. 375, 377.
- Jenner's shipment "of many years before" was unopened when Balmis arrived. Smith, "The 'Real Expedición'" (n. e), p. 61; Archivo General de Indias de Sevilla, Indiferente General, Legajo, IG 1558A, Balmis to Caballero, Lisbon, 14 August 1806.
- ^mSmith, "The 'Real Expedición'" (n. e), pp. 60–61; Ramírez Martín, *La mayor hazaña* (n. e), p. 379.

Table 2 (*continued*). Chronology of First Successful Smallpox Vaccinations, by Geographic Area

^a The report of a single successful vaccination performed by Nariño in Bogotá in 1802 is suspicious, since there is no mention of further distribution. Ramírez Martín, <i>La mayor hazaña</i> (n. b.), pp. 303–4.
^b <i>Ibid.</i> , p. 394.
^c <i>Ibid.</i> , pp. 329–30.
^d Date of arrival in La Paz: <i>ibid.</i> , p. 264.
^e First vaccinations in Chile, Enrique Laval Manríquez, “La viruela en Chile,” <i>Anales Chilenos de Historia de la Medicina</i> , 1967–1968; 9–10: 203–76, pp. 239, 246–51; expedition dates, Ramírez Martín, <i>La mayor hazaña</i> (n. b.), pp. 417–19.

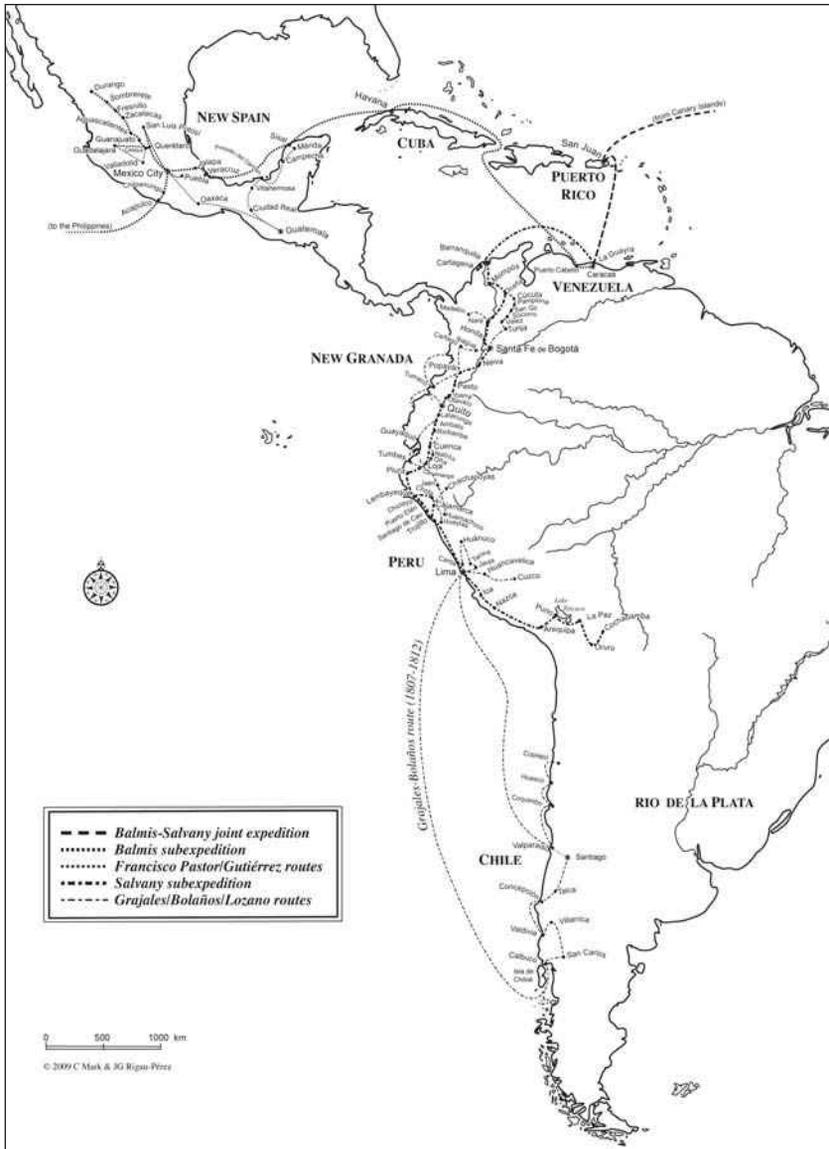


Figure 2. Routes of the Balmis and the Salvany Subexpeditions in the Americas.

teous reception they nevertheless received, the orderly progress of the vaccination program instituted by Dr. Tomás Romay, his cooperation, and the recent success in Venezuela appear to have influenced Balmis's reaction. He reviewed the vaccination program, congratulated Governor Someruelos and Dr. Romay on their accomplishments, and submitted his

proposal for a central vaccination board (which, with the patronage of the Havana Economic Society, would operate successfully for many years).²⁴

From Havana, they sailed to the Mexican ports of Sisal and Veracruz (June–July 1804), once more in the wake of the vaccine, which had arrived weeks earlier from Cuba. Here they found no comprehensive strategy, however; vaccine distribution was unsystematic, and adequate supervision was lacking.²⁵ Although frustrated by the loss of priority in this important component of the monarchy, Balmis set out with his usual tenacity to institute the full program, safeguard the vaccine, and manage its continued distribution.

Between June 1804 and February 1805, Balmis and his aides vaccinated susceptible people and trained physicians in Mexico City and in most major and many minor cities and towns of New Spain, from Mérida and Veracruz in the east to Guadalajara in the west and Durango in the north. Secondary missions were sent to Tabasco, Oaxaca, Chiapas, and Guatemala, and local expeditions soon reached Sonora, Chihuahua, and Texas. Despite heated disputes between Balmis and Viceroy José Iturrigaray, expedition members collaborated with local political, medical, and religious authorities to establish a network of vaccination boards and clinics. It is estimated that the expedition immunized at least 100,000 people in Mexico, most of whom were children (the age group most likely to be susceptible to smallpox).²⁶

With their objectives in New Spain achieved, in February 1805 Balmis and his staff sailed from Acapulco for the Philippines aboard the *Magallanes*, accompanied by twenty-six Mexican boys as vaccine carriers. The parents entrusted their sons to the expedition for monetary compensation and the promise that they would be returned. Conditions on board were deplorable, with dirty, crowded quarters and miserly rations; only the generosity of other passengers and a rapid crossing allowed the expedition to avert misfortune.²⁷ Vaccinations began within a day of the expedition's arrival in Manila (April 1805). Balmis soon left Manila for reasons of health and appointed Gutiérrez to lead the work in the Philippines. Before the expedition's return to Mexico in 1807, some of the staff traveled throughout the islands, including Cebú, Mindanao, and the

24. Smith, “*Real Expedición*” (n. 15), pp. 22–23; José López Sánchez, *Vida y obra del sabio médico habanero Dr. Tomás Romay Chacón* (Havana: Librería Selecta, 1950), pp. 121–30.

25. Patricia Aceves Pastrana and Alba Morales Cosme, “Conflictos y negociaciones en las expediciones de Balmis,” *Estudios Hist. Novohispan.* 1997, 17: 171–200.

26. Smith, “*Real Expedición*” (n. 15), p. 49.

27. AGI, IG 1558A, Balmis to Caballero, Manila 18 August 1805.

Visayas, where vaccinations exceeded 20,000.²⁸ A vaccination board was established in the capital.²⁹

Balmis sailed to the Asian mainland (September 1805), reestablished vaccination in the Portuguese colony of Macao, where it had been introduced and lost earlier that year, and created a vaccination board. Together with Manila's, this board would supply vaccine to neighboring areas for years to come.³⁰ In Canton (Guangzhou, China), when agents of the Spanish Royal Philippine Company refused their support, Balmis turned to the British East India Company, which provided aid and a vaccination center. In one of history's sad ironies, the date of this British–Spanish cooperation coincides almost exactly with the decisive confrontation between these powers at Trafalgar (October 1805). Balmis returned to Europe aboard a Portuguese frigate, stopping briefly at the island of St. Helena (June 1806). He landed in Lisbon in August and was received triumphantly at court by King Carlos IV in September 1806.

Balmis was appointed inspector general of the vaccine for Spain and the Indies and continued to work toward the prevention of smallpox. Spain was soon engulfed by the Napoleonic invasion, but Balmis was sent to Mexico once more (1810) to reintroduce the vaccine where it had been lost and to search for an indigenous source of cowpox. While in Valladolid de Michoacán (now Morelia), he noticed (he later claimed) the preparations for the uprising of 16 September 1810 that initiated Mexico's War of Independence and quickly returned to Mexico City. In August 1811, while he waited in the city of Xalapa to depart from the port of Veracruz, the insurgents invaded the region. By his own account, Balmis was the only physician and surgeon available to treat the civilians, the royalist defenders of the city, and the captive wounded insurgents.³¹ In 1813 he returned to Spain; he was named chamber surgeon by Fernando VII (1815), elected to the Royal Academy of Medicine (1816), and died at sixty-five years old in Madrid in February 1819.³²

28. Smith, “*Real Expedición*” (n. 15), p. 58.

29. Thomas B. Colvin, “Arms Around the World: The Introduction of Smallpox Vaccine Into the Philippines and Macao in 1805,” *Revista de Cultura*, 2006, 18, 70–88.

30. C. Michele Thompson, “The Nguyen Initiative to Acquire *Vaccinia*, 1820–1,” in *Acta: First International Conference on History of Medicine in Southeast Asia*, ed. Harold J. Cook and Laurence Monnais. Wellcome Series in the History of Medicine (Amsterdam: Rodopi, in press), ch. 8.

31. Smith, “*Real Expedición*” (n. 15), p. 62; Moreno Caballero, *Sesión apologética* (n. 11), pp. 34–35.

32. Susana M. Ramírez Martín, *La mayor hazaña médica de la colonia. La Real Expedición Filantrópica de la Vacuna en la Real Audiencia de Quito* (Quito, Ecuador: Ediciones Abya-Yala, 1999), p. 287.

The Salvany Subexpedition

Salvany's retinue traveled a considerably more arduous route than Balmis's group; they faced the distances, punishing terrain, and harsh climates of the Andes, and Salvany soon began to experience the ill health that would accompany him for the remainder of the journey (Fig. 2). Difficulties began when their brig ran aground in the mouth of the Magdalena River (May 1804), although passengers and vaccine were rescued. In the course of their travel and faced with local smallpox outbreaks, the group divided frequently to visit cities, villages, and settlements, often assisted by local missionary friars. They vaccinated and taught the technique to physicians and laypeople in a path down the western side of the South American continent. Following the river from Cartagena, they reached Bogotá in December, directed eight general vaccination sessions, and established boards for the prevention of smallpox and yellow fever in New Granada.³³ In March 1805, they began the journey south through the Andes, to Neiva, Popayán (May 1805), Pasto, Ibarra, Quito (July 1805), Ambato, Riobamba, Cuenca (October 1805), Loja, Piura (December 1805), Trujillo, Lambayeque, Cajamarca, and Lima, where they arrived in May 1806.

The vaccine had been introduced in the Peruvian capital from Buenos Aires the previous year. Vaccine from Portugal had arrived in Bahia (Brazil) at the end of 1804, reached Rio de Janeiro the following May, Montevideo in July, and Buenos Aires in August.³⁴ Dried vaccine lymph was then sent to the inland provinces and, by boat, to Santiago de Chile, where successful vaccinations were obtained in October 1805. Almost simultaneously, vaccine was propagated in Lima from samples sent by overland mail from Buenos Aires.³⁵ Salvany was chagrined to find that vaccine distribution was haphazard and that some local physicians were making handsome earnings through fees charged for vaccination. While in Lima, he presented his doctoral dissertation at the University of San Marcos (November 1806).

Salvany traveled to Cuzco, Ica, Nasca, and Arequipa (September 1807). He was forced to halt in Puno, on the shores of Lake Titicaca, in September 1808 to recover from a heart ailment, but then continued on to

33. AGI, IG 1558A, extract of letter from Viceroy Amar, Bogotá, 19 June 1805.

34. Isabel Morais, "Smallpox Vaccinations and the Portuguese in Macao," *Review of Culture*, 2006, 18: 113–24; Ramírez Martín, *La mayor hazaña* (n. 32), p. 323. Vaccine transportation from Brazil to Angola was not successful until 1819; see Dauril Alden and Joseph C. Miller, "Out of Africa: The Slave Trade and the Transmission of Smallpox to Brazil, 1560–1831," *J. Interdiscip. Hist.*, 1987, 18: 195–224, esp. pp. 211–12.

35. Ramírez Martín, *La mayor hazaña* (n. 32), pp. 323–25; Lastres, *La salud pública* (n. 8), p. 55.

the territory of the viceroyalty of Buenos Aires. His last report (La Paz, March 1809) indicated that there had been nearly 200,000 vaccinations in Peru. He included a medical certificate documenting his extremely poor health but nevertheless outlined plans to continue the expedition. His 4,000-kilometer progress through half of South America by boat, horse, and mule; on foot; and even on the backs of human porters came to an end in Cochabamba, present-day Bolivia, where he died in July 1810.³⁶ Grajales and Bolaños carried the vaccine from Lima to Chile, arriving in Valparaíso in December 1807. Four years and a revolution later,³⁷ they sailed from southern Chile for the Peruvian port of El Callao, concluding the South American expedition in 1812.

From “Last Conquistador” to “First Vaccination Campaign”

By 1804, six years from the publication of Jenner’s discovery, vaccine lymph had spread through Europe and reached the Americas, India, China, the East Indies, and Australia through the agency of enterprising individuals, societies, and government officials. The Philanthropic Smallpox Expedition is usually mentioned only as part of that progress, in terms of the history of smallpox or smallpox vaccination. One of the first books based on comprehensive research on the expedition’s voyages (Díaz de Yraola, 1948) opens with an invocation of adventure, discoverers, and conquistadors.³⁸ The expedition in fact represented the world’s first vaccination campaign in that it possessed the modern characteristics of such a project: it was centrally planned and executed by specialized staff assigned exclusively to the subject, with goals that included short-term broad coverage of populations and geographic areas and long-term institutionalization of vaccine services.

Vaccination campaigns designed to quickly protect large populations in remote areas are a recent development in public health, made possible by technological improvements but especially by the success of the World Health Organization’s smallpox eradication campaign (1967–80) and the 1977 World Health Assembly’s resolution to pursue “Health for all by the year 2000.”³⁹ It is therefore not surprising that the historiography of the

36. Miguel Parrilla Hermida, “Biografía del Doctor José Salvany Lleopart,” *Asclepio*, 1980, 32: 303–10.

37. Ramírez Martín, *La mayor hazaña* (n. 32), p. 419.

38. Gregorio Marañón, “Prologue,” in Díaz de Yraola, *Vuelta al mundo* (n. 11), pp. 7–12.

39. Basch, *Vaccines and World Health* (n. 2), pp. 40–45.

Royal Expedition offers only one source that (very succinctly) compares it to a modern campaign. The Venezuelan physician-historian Ricardo Archila called it, in 1969, “one of the pioneers among sanitary measures at an international scale, distinguished as the first [centrally] directed, systematic campaign with epidemiologic considerations.”⁴⁰

Unquestionably, large numbers of people were vaccinated before the Spanish expedition as a result of the introduction of vaccination in the British army and navy in 1800 (not compulsory until 1802 and after 1811, respectively) and in British India starting in 1802.⁴¹ Operations in the military are very different from campaigns in civil society, but the vaccination of Indian civilians may have been more in the nature of a campaign. One of the earliest ventures was the shipment of vaccine eastward via Baghdad and Basra to India, where it arrived in 1802.⁴² Although cursory comparison suggests similarities with Spain’s initiative, the combination of political and social factors created very different contexts for the Spanish and British introductions.

Smallpox was an “old,” endemic disease in India. Both the illness and its treatment had long figured in customs and beliefs and were associated with specific deities.⁴³ Inoculation was an established practice in parts of the subcontinent; attempts to replace it with vaccination had both economic and quasi-religious implications and therefore met with more resistance there than it did in Spanish America.⁴⁴ Imperial control had yet to be consolidated; in the early 1800s British India was still the dominion of the East India Company, which shared political and administrative responsibilities with the British government. Vaccine introduction in India was not initially conceived as an organized campaign and at first relied as much on individual dedication and local contacts as on official means.⁴⁵

40. Ricardo Archila, “La Expedición Balmis en Venezuela [Parte I],” in *IV Congreso Panamericano de Historia de la Medicina* (Guatemala: Ministerio de Educación, 1970), pp. 171–203, esp. 173.

41. A. M. Ward, “Smallpox and Vaccination in the Armed Forces From the Eighteenth Century Onwards,” *St. Bartholomew’s Hospital Journal*, 1960, 64: 197–99; John S. Keevil, *Medicine and the Navy*, 4 vols. (Edinburgh: E & S Livingstone, Ltd., 1957–1963), 3: 350–51; and Niels Brimnes, “Variolation, Vaccination and Popular Resistance in Early Colonial South India,” *Med. Hist.*, 2004, 48: 199–228.

42. John Z. Bowers, “The Odyssey of Smallpox Vaccination,” *Bull. Hist. Med.*, 1981, 55: 17–33; Michael Bennett, “Passage Through India: Global Vaccination and British India, 1800–05,” *J. Imp. Commonw. Hist.*, 2007, 35: 201–20.

43. David Arnold, “Smallpox and Colonial Medicine in Nineteenth-Century India,” in *Imperial Medicine and Indigenous Societies*, ed. David Arnold (Manchester: Manchester University Press, 1988), pp. 45–65; Bowers, “The Odyssey of Smallpox Vaccination” (n. 42), pp. 23–24.

44. Arnold, “Smallpox and Colonial Medicine” (n. 43), p. 56.

45. Bennett, “Passage Through India” (n. 42), pp. 201–20.

Schemes for government control were initiated soon thereafter, however; by 1803, the Madras Presidency had published a plan and was training vaccinators.⁴⁶ It was therefore a government program for a limited area quite unlike the scope of the Spanish expedition.

As it had been introduced to the Americas relatively recently, smallpox held no place in the ancestral belief systems or customs of the indigenous peoples in Spanish America, and vaccination thus did not supplant an existing tradition. Spain's three-century-old political authority was firmly established, and its well-organized military, ecclesiastical, judicial, and medical infrastructures equipped it for carrying out such a campaign. The king and the Council of the Indies considered that administrative control of vaccine distribution in the overseas territories was a responsibility of the state, to be supported by its institutions at all levels. To broaden the spatial and temporal scope of vaccine distribution, from the beginning the plan included establishment of permanent institutions for disease control in the form of centrally organized and supervised vaccination boards, each of which had regulations adapted to local needs and circumstances.⁴⁷

Constants in Vaccination

Alexandra M. Stern and Howard Markel have remarked on the continuing importance, since Jenner's day, of specific technical, financial, and social issues that affect the impact of any immunization program.⁴⁸ The frequency of dissension between local authorities and the expedition staff members indicates the conceptual novelty and the administrative and political difficulties presented at that time by still-important issues surrounding the introduction of new immunizations, such as efficacy, safety, cost, control, coverage, technology transfer, and the protection of human subjects. Many of the disagreements along the expedition's voyages have been attributed to Balmis's arrogance. From our perspective, however, the controversies can be seen less as due to personal conflicts than to the development of professionalization in public health. Balmis claimed preeminence for the opinion of the expert over that of the local military authority or even local medical staff.

46. Brimnes, "Variolation, Vaccination and Popular Resistance" (n. 41), pp. 202–3.

47. Ricardo Archila, "The Balmis Expedition in Venezuela. Part II: Founding of the Central Vaccination Board, 1804," in *Aspects of the History of Medicine in Latin America*, ed. John Z. Bowers and Elizabeth F. Purcell (New York: Josiah Macy, Jr. Foundation, 1979), pp. 142–81; Susana M. Ramírez Martín, "El legado de la Real Expedición Filantrópica de la Vacuna (1803–1810): las Juntas de Vacuna," *Asclepio*, 2003, 56: 53–61.

48. Alexandra M. Stern and Howard Markel, "The History of Vaccines and Immunization: Familiar Patterns, New Challenges," *Health Affairs*, 2005, 24: 611–21.

Clinical Issues

The major subject of argument throughout the expedition's travels was the quality of local vaccine. This issue has been crucially important in every vaccination campaign ever since. At present, efficacy is proven before vaccine licensure in large clinical trials that compare the incidence of natural disease in vaccinated and unvaccinated people. The use of "controls" was not a common practice at the time of the expedition.⁴⁹ Balmis's own work on the value of the agave and begonia plants for treatment of syphilis, published in Madrid in 1794, did not incorporate the idea of comparative testing.⁵⁰ Whenever the question of efficacy came up, Balmis and his generation tried, on a patient-by-patient basis, to determine whether the person had become immune to smallpox or had produced a typical vaccination reaction (which "proved" that prior vaccination was "false" or ineffective).

The absolute safety of the vaccine is never questioned in the expedition's documents. Like most vaccinators in his generation, Balmis was practically blind to the possibility of serious side effects.⁵¹ Nevertheless, there were two potential causes of problems: the infection itself and the method with which it was disseminated. Balmis and his contemporaries (until about 1814) failed to see that the arm-to-arm method served to transmit other diseases, such as erysipelas, syphilis, and hepatitis.⁵² The expedition's necessarily rapid pace (spreading vaccine, instructing practitioners, establishing a vaccination board, and moving on) allowed little opportunity for detecting such problems.

Administrative Issues

Funding for the expedition's services was the vaccinators' other important source of disagreement with local authorities. Their parsimony has been attributed, with reason, to limited means and the prior arrival of small-

49. Abraham M. Lilienfeld, "Ceteris Paribus: The Evolution of the Clinical Trial," *Bull. Hist. Med.*, 1982, 56: 1–18.

50. Francisco Xavier de Balmis, *Demostración de las eficaces virtudes nuevamente descubiertas en las raíces de dos plantas de Nueva-España, especies de ágave y de begonia, para la curación del vicio venéreo y escrofuloso y de otras graves enfermedades que resisten al uso del mercurio y demás remedios conocidos* (Madrid: Viuda de Joaquín Ibarra, 1794).

51. Even after all the vaccinations he conducted around the world, Balmis indicated to Minister Caballero in Madrid (AGI, IG 1558A, 12 February 1807) that "vaccine . . . did not cause the least harm, the least risk, to those who received it."

52. Donald R. Hopkins, *Princes and Peasants: Smallpox in History* (Chicago: University of Chicago Press, 1983), p. 85.

pox vaccine at a critical time in the empire's economy. Nevertheless, we must move beyond anecdote to underscore a constant tension in public health efforts: it is difficult to persuade society that the cost of vaccination (for any disease) represents a wise investment and a long-term savings. In our day, cost-effectiveness studies are conducted to examine the benefits derived from vaccination and to produce economic arguments that will convince policymakers. Although Carlos IV apparently decided with his heart, rather than his pocket, on the need to send the expedition to America, his bureaucrats in Madrid reasoned that the benefit for the most severely affected populations, the Native Americans, would result in greater income for the Treasury.⁵³

Until recently, accounts of the Spanish expedition focused on a protagonist, Francisco Xavier de Balmis, and his journey around the globe from 1803 to 1806. In truth, the mission was a ten-year institutional effort, from its planning in early 1803 to Balmis's return from Mexico in 1813. This was also the contemporary institutional view; Spain's government continued to pay the salaries of the staff for most of that decade, and Balmis held the position of director up to 1813. The single focus on Balmis's leadership has been reinforced by his own protestations in documents, by acceptance of staff hierarchy as an indication of individual capability, and by a lack of understanding of the fluidity of professional roles in a field operation. In fact, the expedition profited as much from central planning as it did from decentralization of local activities. The specially trained men who held subordinate positions titled "assistant" or "practitioner" were nevertheless able to show an extraordinary capacity for independent good judgment and hard work, because the campaign operated as a collection of groups in simultaneous action. Our current knowledge of the personal and professional lives of its staff is summarized in Table 1. There was, in addition, the "home base" in Madrid, where the bureaucrats received reports and from which they sent funds, books, or admonitions to local authorities.⁵⁴

Transfer of vaccine-related technology was very important for Balmis. We have compared the expedition to a modern vaccination campaign,

53. AGI, IG 1558A, Opinion of the President of the Council of the Indies, Marqués de Bajamar, 26 May 1803.

54. Previous historians of the expedition have not mentioned that the documentation in the AGI, IG 1558A also contains the notes and comments of Mssrs. León and Salcedo, the clerks in charge of correspondence. Balmis, in a letter to Viceroy Venegas (Mexico, 31 January 1811) mentions one of them: "Mr. Antonio Salcedo, senior official at the Secretaría de Gracia y Justicia, through whose desk our expedition is handled" (Archivo General de la Nación, Mexico, Epidemias, vol. 17: 250).

but it could also serve as an example of technology transfer writ large: the processes and consequences of moving technological ideas, skills, procedures, hardware, and systems across a variety of boundaries.⁵⁵ Four phases have been proposed: decision to pursue the introduction of the new method; acquisition; innovation or first local use; and diffusion.⁵⁶ Vaccine was so desirable a product that the “decision to pursue” was made both in Madrid and in the periphery, as attested by the many efforts to import it before Balmis’s arrival. Acquisition includes not only equipment but also expertise, a need Balmis addressed in two ways. Although vaccination manuals had circulated in the Americas for years, Balmis freely distributed his translation of Moreau’s book to ensure strict adherence to Jennerian practice. Then he offered clinical demonstrations, described by a surgeon in Puerto Rico as “long conferences” given “chair to chair to make us see physically . . . when the vaccine pustule is ripe,” which suggests that Balmis would sit next to the trainee, facing a vaccinated child.⁵⁷ Innovation with success demands mastery in maintenance and repair of the new method. Diffusion, or the replication of the innovation over time and geography, requires the multiplication of technicians and equipment. This temporal sequence is embedded in a context of social and physical forces that provide assistance or resistance to the adoption of the new system. For example, many local physicians were trained by the expedition, but they were expected to maintain the viable vaccine chain without any special support from the impoverished state—one of the reasons why, in some locations, vaccine became unavailable shortly after its introduction. Innovation gives prominence to new social actors, such as technicians, regulatory officials, and consumers. As mentioned above, conflicts between these groups and a hierarchical society in severe tension characterized the march of the campaign. In the context of the wars of independence, vaccination boards, and even vaccine, were frequent casualties. The perceived benefits, the requirements, and the demand for the new method changed in the years after the expedition.

55. Bruce E. Seely, “Historical Patterns in the Scholarship of Technology Transfer,” *Comparative Technology Transfer and Society*, 2003, 1: 7–48; esp. p. 8.

56. Edward Beatty, “Approaches to Technology Transfer in History and the Case of Nineteenth-Century Mexico,” *Comparative Technology Transfer and Society*, 2003, 1: 167–200, on which the rest of the paragraph is based.

57. AGI, Audiencia de Santo Domingo, Legajo 2322, deposition of Juan Antonio Dorado, surgeon of the San Juan (“Fixed”) Regiment, 1 March 1804.

Epidemiologic Issues

It is estimated that the expedition vaccinated 100,000 persons in New Spain, perhaps twenty percent of those who might have benefited from vaccination.⁵⁸ Grajales claimed to have personally reached over 400,000 vaccinees in close to a decade of work from the Caribbean to Patagonia.⁵⁹ Expedition staff took a great many detours to small villages that were peopled mostly by natives to ensure that vaccine reached rural areas where smallpox outbreaks posed a risk to life (a precursor approach to action guided by surveillance). The staff took care to report the number of vaccinated persons (a process measure) and how, on occasion, they were able to control an outbreak (disease incidence). Nevertheless, we lack complete figures for vaccinations, total population, proportion of susceptible people, frequency of vaccination by class or racial origin, and frequency of smallpox cases in the succeeding years with which to ascertain the expedition's results. Although the estimate of coverage of twenty percent for New Spain may seem insufficient, the realistic goal would have been far below one hundred percent, considering this was an itinerant expedition using a new method that required that not all susceptible people be immunized (so that vaccine could be kept alive by arm-to-arm transmission). In contrast, the Rio de Janeiro municipal vaccine commission surpassed 100,000 vaccinees only after two decades of operation.⁶⁰ The protection of hundreds of thousands of vaccinees from infection or at least severe smallpox was a colossal achievement for the time.

Ethical Issues

The boys who sailed with the expedition in 1803 were foundlings, that is, they had been abandoned at birth, and someone had taken them to an asylum. On arrival the survivors were fed, clothed, and cared for, but a few days later, they were sent to live with adoptive families. Lactation, in exchange for meager pay, was one of the obligations of peasant mothers in northwest Spain, a system that was also used in early nineteenth-century France.⁶¹ The king promised special protection and education in a school in Mexico for the children who participated in the expedition, which was a great improvement on their regular expectations. Undoubtedly,

58. Smith, "Real Expedición" (n. 15), p. 49.

59. Ramírez Martín, *La mayor hazaña* (n. 32), p. 419.

60. Alden and Miller, "Out of Africa" (n. 34), p. 112.

61. Ann F. La Berge, *Mission and Method: The Early Nineteenth-Century French Public Health Movement* (New York: Cambridge University Press, 1992), p. 272.

the boys were well treated; after all, the vaccination chain depended on their health, and their appearance had to impress favorably the parents of potential vaccinees. Even so, four (six percent) of the sixty-two children who took part in the different sea voyages died. There was recognition that all children, including the foundlings, deserved a standard of care that included good food, clothing, and motherly attentions (that's why Isabel Zendala went with the expedition). Nevertheless, as shown by the attempt to test the efficacy of "goat pox" in foundlings in Madrid (stopped by the foundling home's Ladies' Board of Directors), state officials showed no hesitation in using wards of the state as tools with which to improve public health.⁶²

In spite of the extraordinarily large number of vaccinations performed, letters to Madrid frequently reported local resistance to the expedition's efforts. The small group of educated officials, clerics, and professionals in Spanish American society was disposed to accept the method. Vaccination enjoyed the personal support of the king, his government, and prominent local churchmen, and the expedition enlisted the power of their prestige to encourage the public to take the vaccine. Once the first wave of volunteers was vaccinated, though, the expedition and succeeding Juntas de Vacunación faced the passive resistance of a large proportion of the population, out of, perhaps, fear of pain, distrust of governmental measures, indolence, inconvenience, or skepticism (there was, after all, no precedent in history for such a simple and effective preventive procedure). Salvany experienced such incredulity in Chocote, a "pueblo de indios" near Lambayeque (Peru) in January 1806. Although the inhabitants had invited him to come vaccinate them, the simplicity of the operation they saw made them doubt its effects. They accused Salvany of lying and being "the anti-Christ." He tried to convince them of the efficacy of the vaccine but reported, "although Indians are very simple and satisfied with little, they doubt everything, and especially that which the White Man proposes" so they remained "not very satisfied" by his explanations.⁶³

Vaccination was voluntary, but to maintain the arm-to-arm vaccine chain, the expedition's staff occasionally forced the vaccine on unwilling subjects. On arrival in Veracruz (Mexico) in July 1804, Balmis found no volunteers to submit to the procedure because vaccine had been introduced from Cuba in April. Ten recruits from the local regiment, procured

62. Susana M. Ramírez Martín, "Juan José Heydeck, un alemán en la corte de Carlos IV: experimentos contra la viruela," *Asclepio*, 2006, 58: 165–202.

63. AGI, IG 1558A, José Salvany to Antonio Caballero, Lima, 1 October 1806. This episode is entirely misrepresented in Díaz de Yraola, *La vuelta al mundo* (n. 11), p. 181.

by the governor, were then vaccinated.⁶⁴ A similar situation in Mexico City in August forced a municipal official to “compel” twelve individuals to submit to vaccination. Lymph from these vaccinees was transmitted because the same official “dragged in twenty Indian women whose children were vaccinated only after a thousand entreaties . . . Then every single one immediately went to the closest apothecary to get an antidote for the poison that had been introduced into their children’s arms.”⁶⁵ There was also some active resistance locally, not to the vaccine, but to the work and demands of the expedition. Institutions and officials were reluctant to provide the funds, attention, and respect that the expedition required, at a time when the economies of Spain, its viceroyalties, and even cities were exhausted by the demands of war. The knowledge of such institutional objections might also have affected some individuals’ decision to accept vaccination.

Conclusion

Although the overall itinerary of the expedition is by now well established, there are important gaps in our knowledge of its activities and effects. No contemporary drawing or painting that we know portrays participants or their work. The expedition’s documentary sources are scattered throughout the world and even within countries and archives. The most complete list of documentary sources published so far is in Ramírez Martín’s work, which covers archives in Spain, Venezuela, Ecuador, and Bolivia.⁶⁶ Other researchers have worked with documents in the national repositories of Mexico, Cuba, Puerto Rico, Venezuela, Peru, and Chile, but we know of no accounts based on the central archives of Colombia or the Philippines. The local records of Puebla (Mexico), Cuzco (Peru), Oruro, and Cochabamba (Bolivia) may hold interesting findings, as these are the last known locations of principal expedition staff. The concerns and observations of Balmis and his associates are scattered in mentions throughout hundreds of manuscript pages. Their transcription to electronic format, so that specific words and phrases can be easily searched, will allow a dif-

64. Smith, “*Real Expedición*” (n. 15), p. 32.

65. *Ibid.*, p. 35.

66. Ramírez Martín, *La mayor hazaña* (n. 32), pp. 585–664. See also Ramón Navarro García, “Análisis de los documentos esenciales sobre la Real Expedición de Balmis-Salvany,” in Ramírez et al., *La Real Expedición Filantrópica de la Vacuna* (n. 11), pp. 61–75, and additional documentary sources in Susana M. Ramírez Martín, “Los perfiles de Francisco Xavier Balmis,” in *La colección Balmis del Real Jardín Botánico. Retorno ilustrado del viaje a Oriente de la Expedición de la Vacuna (1803–1806)*, ed. María Pilar de San Pío Aladrén (Madrid: Lunwerg Eds., 2006), pp. 31–53.

ferent reading of these documents, which so far have been considered mainly as reports of geographic coverage. Local studies are also needed to measure the impact of the expedition on the health of the population. An examination of smallpox prevention activities in Mexico, in Guanajuato from 1797 to 1840 and in San Luis Potosí from 1805 to 1821, shows that, contrary to expectations, vaccine services were not always a quick casualty in the wars of independence. Guanajuato succeeded in preserving the vaccine and avoided smallpox epidemics for twenty-five years after the expedition's arrival,⁶⁷ and vaccination continued in San Luis Potosí, albeit irregularly, until 1821.⁶⁸

The Royal Philanthropic Vaccine Expedition represents an extraordinary administrative and sanitary achievement. In remote locations, individuals, or even local institutions, would not have been able to overcome the obstacles to the transport of viable vaccine over long distances, often far from the usual routes of maritime or land transportation. Smallpox eradication would have to wait until the second half of the twentieth century for the establishment of ordered infrastructures supported by a synchronized system of local, national, and international institutions.⁶⁹ Balmis and the Spanish authorities perceived the need for such coordination and made use of mechanisms that would, in time, be considered essential components of an effective vaccination campaign. Their farsighted approach in the planning of the 1803 expedition differed considerably from other early mass vaccination programs in Europe, the Americas, and Asia, and allowed them to establish appropriate procedures for delivering and maintaining vaccine supplies for the benefit of the population.⁷⁰



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67. Angela T. Thompson, "To Save the Children: Smallpox Inoculation, Vaccination, and Public Health in Guanajuato, Mexico, 1797–1840," *The Americas*, 1993, 49: 431–55.

68. Ana Irisarri Aguirre, "La vacunación contra la viruela en la provincial de San Luis Potosí tras la expedición de Balmis: 1805–1821," *Fronteras de la Historia*, 2007, 12: 197–226.

69. Ann Jannetta, *The Vaccinators: Smallpox, Medical Knowledge, and the "Opening" of Japan* (Stanford, Calif.: Stanford University Press, 2007), pp. 25–52.

70. An international group of scholars interested in the Balmis-Salvany expedition maintains a forum for discussion and comment, information postings, queries, document and file exchange, etc. Participation is welcomed; the site can be found at <http://groups.yahoo.com/group/balmis/>

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