The Spanish Royal Philanthropic Expedition to Bring Smallpox Vaccination to the New World and Asia in the 19th Century

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The New World was ravaged by smallpox for several centuries after the Spanish conquest. Jenner’s discovery of the smallpox vaccine made possible the prevention and control of smallpox epidemics. In response to a large outbreak of smallpox in the Spanish colonies, King Charles IV appointed Francisco Xavier de Balmis to lead an expedition that would introduce Jenner’s vaccine to these colonies. During the journey, the vaccine was kept viable by passing it from arm to arm in orphaned children, who were brought along expressly for that purpose and remained under the care of the orphanage’s director. This expedition was the first large scale mass vaccination of its kind. The historic legacy of this pioneering event in international health should be revisited in the current era of persistent inequalities in global health.

SMALLPOX IN THE NEW WORLD

Smallpox infection was introduced to the Western Hemisphere during the 16th century by an African slave who was a member of the Spanish expedition led by Panfilo de Narvaez in 1520 [1–6]. Dissemination of the smallpox virus among Aztec and Inca populations was a decisive factor in the defeat of these grand empires [7, 8]. The catastrophic epidemics that followed during the next 4 centuries caused severe morbidity and mortality among Native American tribes [9]. The Aztec population, which numbered 26 million at the time of the Spanish conquest (1519–1520), declined to ~1.6 million by 1620 [6, 8]. Smallpox is considered one of the leading causes of these demographic shifts [8, 10].

VARIOLATION AND VACCINATION

Many attempts to halt the impact of the smallpox virus have been documented in different countries over several centuries [11–14]. The practice of introducing the content of a pustule from an infected person to a healthy person to protect against subsequent smallpox exposures was known as variolation [11, 12]. Smallpox induced in this manner usually resulted in a milder smallpox infection with fewer lesions than smallpox acquired by inhalation. The practice of variolation extended from China and India to western Asia and Africa, and arrived in England and continental Europe by the mid-18th century [11–13]. Despite the success of this procedure, variolation was responsible for a myriad of unwanted side effects: severe scarring, transmission of the infection to others, and transmission of syphilis, as well as fatal outcomes in nearly 2% of cases [1, 10, 11].

In 1797, Edward Jenner demonstrated that material taken from a human pustular lesion caused by cowpox virus and inoculated onto the skin of another person produced a similar infection [11–13]. He then demonstrated that an inoculated individual was protected from infection with the smallpox virus. Within a decade of his discovery, “vaccination,” the word Jenner invented for this procedure, was at the forefront of the medical and political world [3]. The practice of vaccination spread rapidly, and, by the beginning of the 19th century, it had reached most European frontiers [11–14].

SMALLPOX VACCINATION REACHES THE NEW WORLD

At the end of the 18th century in Europe, during the reign of King Charles IV of Spain, many members of the Bourbon royal family became infected with the smallpox virus [10, 15, 16]. Gabriel, King Charles’s brother, and his sister-in-law, the Portuguese queen Maria Ana Victoria, succumbed to smallpox. In
addition, the king’s daughter, Queen Maria Luisa, and the Princess of Parma were all infected with the smallpox virus but survived [15]. Urged by the queen, King Charles IV ordered that the unaffected members of the royal family should be variolated, and although they survived the procedure, they suffered significant skin scarring [11]. These incidents inevitably attracted King Charles’ attention to the medical and social implications of smallpox, and by 30 November 1798, King Charles IV declared that the civilian population should be variolated [1, 5, 16]. A year later, a copy of Edward Jenner’s book was sent to King Charles IV by an Italian physician, further attracting his attention to the prevention of smallpox [9, 13]. All these events culminated in the issuance of a royal edict announcing the widespread availability of the smallpox vaccine in Spain in 1800 [11].

Two years later, in the New World, a large smallpox epidemic afflicted the population of Santa Fé in New Granada (now Colombia) [1–5, 10, 16]. The viceroy of New Granada pleaded with King Charles IV for help [10, 16]. Other regions in the Americas were experiencing the same fate, with similar concurrent epidemics [16]. Realizing that the Spanish colonies were being devastated by epidemics of incalculable magnitude, the king called for a meeting of the Council of the Indies (Consejo de Indias) [1–3, 10]. Dr. Joseph Flores, the King’s court physician, was consulted on the issue because he was originally from Chiapas, México [1–4, 10]. Dr. Flores’s recommendations included sending a Spanish corvette carrying the vaccine to the New World. The plan to carry the vaccine consisted of the passage of vesicle fluid from child to child. As the skin vesicles began to exude fluid a few days after the initial inoculation, it would be transmitted through skin contact to another child. He also recommended that vaccination campaigns be supervised by the Catholic clergy and that immunization registries be kept by priests. This recommendation was based on the influence and legal authority exerted over the civilian population by the Catholic clergy in the colonial territories [10]. On 22 March 1803, the Council of the Indies approved the resolution and announced that there would be a vaccination expedition to the New World [1, 3, 4, 10].

King Charles IV’s project was undertaken at a politically and socially difficult time in Europe. The philanthropic expedition took place at the time when Napoleon’s armies invaded Spain and the French and Spanish armies were defeated by Nelson in Trafalgar [1, 3–5]. Some medical historians have considered King Charles IV a humanitarian and compassionate king during this politically fraught period, despite his failings as a political figure [3, 10].

King Charles IV of Spain officially signed a royal edict for the philanthropic expedition on 28 June 1802 [1, 5, 10]. The Council of the Indies decided that the most suitable individual to lead the vaccination expedition would be Francisco Xavier de Balmis [17–20]. He was an enthusiastic physician and vaccinator, and had previously traveled to New Spain to collect plants and herbal remedies [1, 4, 5, 10, 16]. What truly made him the most eligible candidate was that he had recently translated the treatise of Moreau de la Sarthe, which concerned the vaccine, into Spanish [10, 20].

Dr. Flores’s recommendations were incorporated into the planning of the expedition [4, 10]. After many deliberations and multiple controversies, the corvette Maria Pita was selected for the expedition [10, 18]. On board the Maria Pita were an undefined number of crew members who were responsible for sailing the corvette, lead by Captain Pedro del Barco y España, as well as the specific members of the vaccination group: Francisco Xavier de Balmis, director; Joseph Salvany, deputy director; 3 assistant surgeons; 2 first aid practitioners; and 4 nurses [1, 4, 10, 18]. In order to preserve the vaccine during the journey, the decision was made to bring 22 orphaned children from La Coruña, 18 of whom were from the charity hospital and the other 4 of whom were from La Coruña Orphanage [10, 21, 22]. The fluid from the skin vesicles of the orphaned children was kept on glass slides sealed with paraffin and subsequently stored using a vacuum technique that used pneumatic machines [10].

The 22 orphaned children were between the ages of 8 and 10 and had neither been infected with the smallpox virus nor been previously vaccinated [10, 22]. They were placed under the supervision and care of Isabel de Zendala y Gomez, the director of the orphanage [1, 4, 10]. She brought her son along so that he, too, could contribute to the mission. In de Balmis’s record of the expedition, he expressed on many occasions his gratitude for the tender care that Ms. Zendala y Gomez, the only female member of the expedition, provided to the orphaned children [10].

The expedition disembarked from La Coruña, Spain on 30 November 1803 (figure 1). De Balmis brought along 500 copies of the Moreau de la Sarthe treatise [1, 4, 10, 16]. The first stop on the westbound expedition was the Canary Islands [10, 16]. De Balmis’s expedition then reached Puerto Rico on 9 February 1804, where he suffered a major disappointment: to his surprise, smallpox vaccination had already been instituted on the island [4, 10]. The vaccine had been previously obtained from the Virgin Islands [1, 4, 10]. He worked with the governor to organize a central vaccination board [1, 4, 10]. Thereafter, in every place they stopped, vaccination boards were established. It was decided that these boards should serve several functions: (1) to educate the population regarding the benefits of the vaccine, (2) to provide local production of the cowpox lymph, (3) to administer the vaccine, (4) to document immunizations and keep registries, and (5) to develop a surveillance system for adverse events [1, 3, 4, 10].

De Balmis headed for Puerto Cabello (now Venezuela), and then traveled to La Guayra (now Venezuela). At this juncture,
he decided to divide his efforts with Joseph Salvany into 2 groups. Salvany was to lead a group through the vice-royalty of Peru, and de Balmis was to travel with the other group across the vice-royalty of New Spain to the distant colonies in the Philippines [1, 3, 4, 10, 16].

**Salvany's expedition route.** Salvany’s group sailed in the *San Luis* towards Cartagena de Indias (Colombia) through the Magdalena River, reaching Santa Fé de Bogotá (Colombia) (figure 1) [1, 3, 4, 10, 16]. As the expedition navigated the Magdalena River, it shipwrecked in Barranquilla (Colombia). The crew found asylum with local natives and began their mission by vaccinating them. They continued their journey, and by 24 May 1804, they reached Cartagena de Indias, where they vaccinated approximately 2000 individuals and established vaccination boards. In order to produce more vaccine to continue the expedition, Salvany vaccinated many cows as he passed through the Province of Santa Cruz de Mompox (Colombia) [10].

At Mompox, the expedition again divided into 2 subgroups and set out in different directions. One subgroup continued the journey to Santa Fé de Bogotá by way of the Magdalena River; the second subgroup traveled through the Ocaña region (Colombia) to reach the Cucuta Valley (Colombia) [1, 4, 10]. Both groups later reconvened in Santa Fé de Bogotá [10]. From Cartagena, Salvany sent the vaccine to Portobelo and Panama. During their rigorous journey in a riverboat up the Magdalena River from the Caribbean coast to Santa Fé, Salvany developed an illness that led to the complete loss of vision in 1 eye [1, 4, 10, 16]. The reunited group left Santa Fé de Bogotá, where they had been welcomed with enthusiasm and gratitude for bringing the vaccine [10]. By this time, Salvany had become ill with pulmonary tuberculosis, which manifested as episodes of massive hemoptysis [1, 3, 10]. It has been suggested that Salvany’s eye disease was also due to tuberculosis [10].

Some of the expedition members were commissioned by Salvany to continue the journey to Quito (Ecuador) and Piura (Peru), where they arrived on 23 December 1805 [10]. The harshness of the journey through rivers and the rugged paths in the Andes in Peru was eased by the welcoming gestures they received in the Native American villages [10, 16]. While they were in Piura, they received written communication from the local authorities of the capital city of Lima, Peru, which stated that vaccination was widely taking place in Lima. The expedition were relieved to hear this. [1, 4, 10]. However, when they reached Cajamarca (Peru) on 9 March 1806, and Lima on 23 May 1806, the expedition did not receive the welcome they were accustomed to [10–12]. The vaccine had been pre-
viously introduced in Lima by the viceroy of Buenos Aires [10]. Salvaný appealed to the viceroy of Peru, but the decrees calling for mass vaccinations in Lima were not heeded. Vaccination had become a profitable business for local physicians, who resented the potential loss of income that would be caused by the expedition. Luckily, a new viceroy arrived in Lima who strongly supported the expedition’s endeavors [10]. More than 197,000 vaccinations were administered in Peru [10, 16]. Salvaný subsequently died of tuberculosis while traveling from La Paz (Bolivia) to Buenos Aires (Argentina) [1, 4, 10].

De Balmis’s expedition route. De Balmis’s group arrived in Caracas (Venezuela), where they vaccinated ~2064 people in a short period of time (figure 1). De Balmis also established a vaccination board that was responsible for procuring the vaccine and distributing it to Maracaibo, Margarita Island, and Cumana (now Venezuela) [1, 4, 10]. The expedition left Caracas on 6 May, after the crew had vaccinated nearly 12,000 people, and arrived in Havana (Cuba), where they found that many Cubans were already being vaccinated [10, 17].

De Balmis’s expedition arrived in Mexico through the port of Sisal in Yucatan on 25 June 1804 [10, 18, 21]. The vaccination mission began on 25 June 1804 in Veracruz and traveled through the Mexican provinces of Oaxaca, Queretaro, Guanajuato, and Guadalajara [1–5, 10]. Vaccination boards were mostly comprised of members of the Catholic clergy who would gather on a weekly basis to review vaccination efforts in the different Mexican regions. Detailed immunization records were kept at the local churches [4, 10].

A royal decree by Charles IV directed the de Balmis expedition to continue to the Philippines [10, 16]. De Balmis left Mexico for the Philippines in a different corvette (name unknown), which sailed from the port of Acapulco (on the Pacific coast of Mexico) in February 1805. For this endeavor, he was accompanied by 25 orphaned Mexican children [4, 10]. The orphaned children from Spain who had been part of the original expedition stayed in Mexico under the supervision of the Bishop of Puebla [10]. Despite the termination of her contract on the Spanish children’s arrival in Mexico, Isabel de Zendalá, Josefina de la Diligencia, decided to continue the journey with de Balmis. This allowed her to care for the Mexican orphaned children on board [10]. The expedition arrived in Manila (Philippines) on 15 April 1805 [1, 16]. It is estimated that close to 20,000 individuals were vaccinated by de Balmis’s crew in the Philippines [10].

After establishing vaccination centers for the production and distribution of the vaccine in different regions, the crew left the Philippines on a Portuguese ship named La Diligencia. It sailed westbound to Macau (now part of China) with 3 children on board who were to preserve the vaccine to promote smallpox vaccination [1, 4, 10].

On the ship bound for Macau, 20 members of the crew died as a result of a storm. It is unclear which specific members of the expedition perished. From Macau, de Balmis’s expedition sailed to Canton (now Guangzhou, China), where he is reported to have widely distributed smallpox vaccination [10]. The records of the expedition from Canton to Lisbon, Portugal only make reference to La Diligencia stopping at the British island of Saint Helena while sailing through the South Atlantic [1, 3, 4, 10]. While on Saint Helena, de Balmis offered the vaccine to the local population, despite the prevailing political rivalry between Spain and England [4, 10]. He returned to Spain in July 1806, and presented his activity reports to the Council of the Indies [4, 16]. A few years after the expedition, de Balmis died, neglected and forgotten [3, 6, 10].

The territory covered by the expedition in the Americas and Asia was not only vast, but also brutally harsh, with dense jungles, mountains, and uncharted rivers [16]. In some places, members of the expedition were received with popular enthusiasm and welcoming celebrations [16]. In other places, they encountered political rivalry, financial interests, or cultural beliefs that thwarted vaccination efforts [6]. Resistance to the introduction of the vaccine continued in some areas. A relevant example of this occurred a few decades after the expedition arrived in Mexico. Because of cultural beliefs and political rivalry in the mountains of Sinaloa and Durango, resistance to vaccinations led to the killing of the nurse Lucia Salcido, a nationally recognized promoter of vaccination in Mexico [6]. It is worth noting that Portuguese sailors attempted similar vaccination efforts in their own colonial territories a few years later, based on the experiences of de Balmis’s expedition [16].

LEGACY OF THE VACCINATION EXPEDITION

Charles IV’s undertaking of this enterprise during an era of political instability and war in Spain is evidence of his philanthropic commitment driven by the growing spirit of enlightenment and advancement of science of the early 19th century [1, 3, 10]. At the same time, it would be irresponsible to ignore the fact that, although de Balmis’s expedition was mostly humanitarian, economic and political motivations were also involved, because it was a time when imperial colonial powers dominated Europe.

It was only 7 years after Jenner’s invention of the smallpox vaccine that the vaccination expedition reached 2 other continents. The passing of vesicle fluid from the ulcerated skin of one child to another child, thereby forming a living transmission chain, may not be an acceptable vaccination method by our current hygienic and professional standards; yet it was a creative and effective way of carrying the vaccine at a time when refrigeration, sterile containment, and asepsis were nonexistent [1, 4, 10, 16].

In retrospect, the expedition achieved relative initial success [1, 4]. Vaccination efforts contributed to the growth of population in the Americas [3, 5]. Nev-
ertheless, it should be noted that smallpox continued to rage the Americas and Asia for more than 100 years after de Balmis’s expedition [5, 9, 14]. However, the practice of smallpox vaccination was intermittently continued. Some organized vaccination campaigns were developed in the Americas in the early 20th century, with some success [2, 5]. These efforts finally paid off; the last identified case of smallpox appeared in Mexico in 1951, almost 155 years after Jenner’s discovery and 150 years of de Balmis’s expedition [1, 3, 5]. Subsequent improvements in smallpox vaccination techniques led the Pan American Sanitary Organization to undertake a continent-wide eradication campaign in 1950 [23].

King Charles IV’s vaccination campaign was visionary, occurring almost 150 years before the World Health Organization and 100 years before the Pan-American Health Organization were established. The success of the expedition was due not just to the heroic perseverance and dedication of those who took part in it, but also in their foresight and focus on public education and the use of local molders of public opinion to help get the message across. In this, the expedition is a model of how an expensive, logistically complex international public health effort can translate advanced medical therapy into local cultural contexts. Historic achievements, such as this smallpox vaccination mission, should inspire the ongoing international efforts to control the plagues of our time.

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References