

Fighting against smallpox around the world. The vaccination expeditions of Xavier de Balmis (1803–1806) and Josep Salvany (1803–1810)

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Only seven years after Edward Jenner introduced the vaccine against smallpox, the enlightened King Charles IV of Spain promoted an expedition to extend the great medical breakthroughs throughout the mainland and to the overseas colonies of his kingdom. As director of this difficult and heroic mission, he appointed Dr. Xavier de Balmis, from Alicante, and as his assistant, Josep Salvany, from Barcelona. Despite very different and sometimes conflicting personalities, both men were driven by a common goal: to fight one of the most terrible scourges of humanity, the cause of extremely high mortality and, in those lucky enough to survive, serious after-effects.

Given the short shelf life of Jenner's vaccine and the lack of conservation methods (cold chain), vaccination, especially in the overseas colonies, had to be done 'arm-to-arm,' using a vesicle that had formed in one vaccinated person to vaccinate another. However, this process could be continued only for 10 days, much shorter than the time needed for a transatlantic journey, which in favorable weather conditions would take at least one month. To overcome this problem, children—especially those from orphanages—were enrolled in the overseas expedition. They became the authentic heroes of this important chapter in the control of infectious diseases. Thanks to them, millions of people in America, the Philippines, and China were able to take advantage of the vaccine.

Colonization expeditions versus scientific expeditions

Following the so-called 'discovery' of America, in the late 15th century, a series of expeditions took place over the following two centuries, usually promoted by the European monarchies, with conquer and colonization as their goals. Through genocide and pillage, the "Europeanization" of most of those lands was achieved.

During the 18th and 19th centuries, another series of expeditions of a completely different nature was organized, the aim of which was to study, describe, and, upon the return of the participants, disseminate novel findings of all types (geological, botanical, zoological, anthropological, linguistic, etc.) to Euro-

peans. The list of these expeditions is very long, but to highlight only five:

1. The Hispano-French **geodesic expedition** designed to measure a meridian arc in the equator in order to compare its length with an arc of the same angle previously measured in Lapland. It was demonstrated that the length of the arc and, consequently, the radius of the Earth, is longer at the equator than close to the North Pole. In other words, our planet is swollen at the equator. This expedition was led by the Frenchman Charles Marie de La Condamine and the Valencian, Jorge Juan (1713–1773).
2. During a **botanical expedition**, its leader, Jose Celestino Mutis, of Cadiz (1732–1808), identified and described two hundred species of plants unknown in Europe. Moreover, he collected a wealth of medical material from American natives, mostly from Colombia, thanks to which many diagnostic, preventive, and healing procedures used by those populations became widely known. With the materials brought from America, Mutis was able to found the Botanical Garden of Madrid.
3. **Medical expeditions** conducted by the Valencian Xavier de Balmis (1753–1819) and the Catalan Josep Salvany (1774–1810), discussed in detail below.
4. The **naturalist expedition** by Alexander von Humboldt (1769–1859) led to many extremely important geographic discoveries, including the fluvial connection between the basins of the Orinoco and the Amazon rivers, and the South Pacific sea current that carries his name. His exceptional physical fitness allowed him to climb, without the advantages of modern mountaineering gear, the Chimborazo Volcano, approximately 6000 meters high, to study its rocks and lichens.
5. The **biological expedition** of Charles Darwin (1809–1882) was the source of his well-known studies of the American fauna, especially in the Galapagos Islands. His observations allowed him to formulate his transcendental theory of evolution and the origin of species, which radically changed the scientific world.

Smallpox in Europe

Smallpox was a highly contagious viral infectious disease transmitted through the respiratory tract and causing severe

outbreaks. The main symptoms were a very high fever and malaise, followed by a typical rash that affected the whole body in different phases: macules, pustules, vesicles, and crusts (or scabs). Unlike chickenpox, in smallpox all the lesions are in the same phase and leave a permanent, often very deforming scar (Fig. 1). It is thought that the disease originated in Southeast Asia and spread to the West over the 14th and 15th centuries, with a mortality estimated at 20 % of those infected and serious after-effects, mainly in the form of blindness and skin deformations, in 30 % of the survivors. Annually, smallpox caused around 400,000 deaths in Europe.

While multiple therapies had been attempted, smallpox had no effective remedy. The only relatively useful, preventive method consisted of inoculating smallpox through a different path (i.e., not respiratory). Thus, fluid from a vesicle from a smallpox-infected person was applied to a previously-made excoriation in the receptor's skin. In China, the dust from the crusts of the smallpox lesion was administered nasally. This procedure, known as variolization or variolation, caused a 'minor' form of smallpox and prevented the acquisition of natural smallpox. The success of this strategy was relative because the minor form had a mortality of 5 %, much lower than the 20 % of natu-

ral smallpox but by today's standards intolerable as a preventive measure for use in previously healthy people.

Smallpox in America

Smallpox came to America in 1520 through a slave servicing the troops of Pánfilo de Narváez, sent by the crown to fight against those of Hernán Cortés. The disease spread suddenly and devastatingly across Mexico and half of the native Indians died from smallpox that same year. Throughout the 17th century, smallpox was prevalent throughout America and was particularly virulent in the Caribbean countries. The years 1780 and 1798 were especially notorious because of massive deadly outbreaks.

The first vaccine

In 1796, a momentous event in the history of medicine and humanity took place. Edward Jenner, an English rural doctor from the county of Gloucester, using only his keen spirit of observation, verified that cows were suffering from a disease similar to human smallpox and that their udders presented vesicles similar to those of smallpox-infected patients. This 'smallpox vaccine' infected the milkmaids, provoking the same vesicles in their hands as in the cow's udders. Most importantly, he verified that none of the milkmaids infected with this smallpox vaccine suffered from human smallpox, even during the most virulent outbreaks.

The next step was to artificially provoke spread of this smallpox vaccine in healthy people. The most logical strategy would have been to take fluid from a cow's vesicle and inject it. But Jenner hesitated, probably out of fear of the fierce criticism he could expect from the Anglican church, accusing him of mixing 'animal nature' with 'human nature,' thus joining that which God had separated. To overcome this obstacle, Jenner took fluid from a vesicle of a milkmaid that had been infected by a cow and used it to inoculate a child. After some time, against all current ethical standards of clinical trials, he inoculated the same boy with fluid from a vesicle of a human-smallpox-infected patient and confirmed that in fact he did not acquire the illness. For the first time in history, there was an effective and safe means to prevent smallpox. It was the first 'vaccine.' (Fig. 2)

The vaccination campaigns

Despite some highly critical and satirical efforts against the vaccine, this effective preventive remedy was enthusiastically accepted and the vaccine was extended quickly to all social classes in Europe. The family of the Spanish King Charles IV had suffered from the scourge of smallpox, as one of his daughters had fallen sick and had been left with terrible facial deformities from the scars. Aware of the discovery of the vaccine, he decided to organize a vaccination campaign throughout the mainland and the overseas colonies.

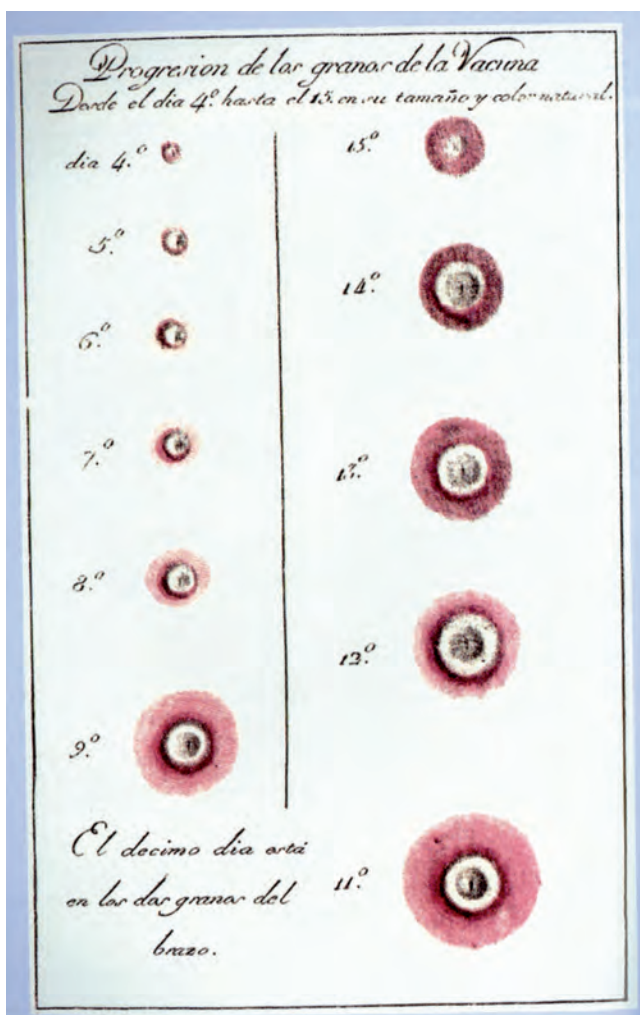


Fig. 1. Propagation of the smallpox scabs from day 4 to day 15 in their natural size and color. Drawing by Valencian artist Juan Ximeno Carro. Historico-medical Library and Museum, Valencia.

The fluid vaccine could be briefly conserved either by soaking a cotton thread in the fluid of a vaccine vesicle, moistening a lancet in the same fluid, or placing a drop of the fluid between two crystals, the edges of which were sealed with wax. Given the lack of mass conservation procedures, particularly a cold chain, the duration of vaccine activity for this fluid was very short, ten days at the most. For mainland territories that period was sufficient to allow mass vaccination of almost the entire population. The problem was the overseas colonies, since a voyage to America would take at least one month under favorable conditions, much longer than the duration of the liquid vaccine's activity. Nor would the period during which active fluid could be extracted from a vaccine lesion, approximately a week, allow the use of one person vaccinated on the mainland

and that same person once American soil was reached. The only solution was to include a group of healthy people on the voyage and vaccinate them sequentially over the course of its duration. Thus arose the idea of organizing a marine vaccination expedition to the overseas colonies.

Organizing the vaccination expedition

Charles IV created a preparatory commission for the expedition, formed by the Court's doctors and surgeons. The expedition, whose official name was the Royal Philanthropic Expedition of the Vaccines (*Real Expedición Filantrópica de la Vacuna*), would have three objectives: (i) to spread the vaccine against smallpox from the Kingdom of Spain throughout all the overseas colonies; (ii) to instruct local health officers in the towns and villages visited in the immunization practice, to ensure its continuity; and (iii) to create a 'vaccination board' to conserve, produce, and supply the vaccine so that the immunization campaign was maintained permanently. The Court dictated announcements so that the scheduled places would know about the arrival of the expedition and could organize human and financial resources for the campaign's success. Local civilian, military, and ecclesiastical authorities were urged to support the expedition and to ensure that the population showed up en masse at the vaccination centers. In most cases, this call was very successful.

The choice for the expedition's director was not controversial. The 50-year-old Xavier de Balmis, a physician from Alicante, was unquestionably the right person (Fig. 3). He was

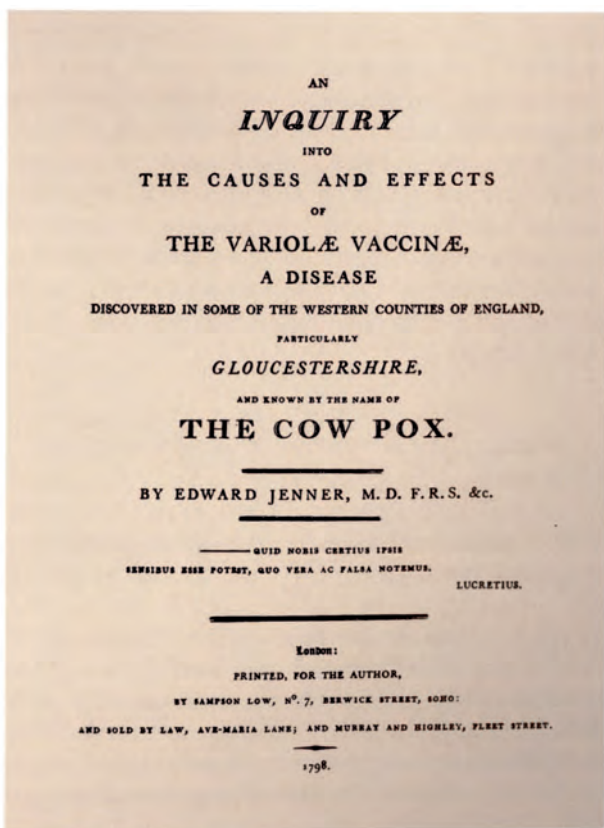


Fig. 2. Top. *An Inquiry Into the Causes and Effects of the Variolæ Vaccinæ, a disease*, by Edward Jenner and published in 1798. Bottom. Sarah Nelmes' hand, with the pustules of cowpox vaccine with which Jenner vaccinated the boy James Phipps on 14 May 1796 (drawing by W. Skelton, colored by W. Cuff).



Fig. 3. Portrait of Xavier de Balmis (1753–1819).



Fig. 4. Balmis' Spanish translation of *Traité historique et pratique de la vaccine* by J.L. Moreau.

highly disciplined, had received solid professional training, and was a good leader. He was familiar with the colonies in America, particularly Mexico, where he had already carried out variolization. Enthusiastic about the vaccine, he had translated the French book by J.L. Moreau de la Sarthe, the highest authority on the subject (Fig. 4). From the beginning, he completely identified with the expedition's objectives. Just after his appointment, in June 1803, he began to meticulously undertake the necessary preparations.

The appointment of the assistant director, however, was controversial. The Court's Board of Physicians and Surgeons felt that the 29-year-old Josep Salvany, from Barcelona, was too young and, compared to Balmis, too different in personality (Fig. 5). He had a solid humanistic education (studies of Latin and grammar) and a great vocation for medicine. He had enrolled in the army as a military health worker and became very skilled in surgical techniques. Balmis did not agree with the choice, but the decisive intervention of the illustrious Catalan surgeon, Antoni Gimbernat, member of the Court's Board of Physicians confirmed the appointment of Salvany as assistant director of the vaccination expedition.

The expedition's medical team was completed by the physicians Manuel Julián Grajales and Antonio Gutiérrez Robredo, the practitioners Francisco Pastor Balmis and Rafael Lozano Pérez, and the nurses Basilio Bolaños, Pedro Ortega, and Antonio Pastor. Obviously, the most important human component, and the basis of the expedition, was still missing: the vaccine carriers.

The vaccine-carrier children, anonymous heroes of the expedition

A group of healthy people who had not been vaccinated or had suffered smallpox had to be chosen. The best candidates were

children between the ages of five and eight. The Crown thus appealed to parents to volunteer their sons and daughters for the expedition. The children were offered free food and clothing and schooling until they found work. Despite this attractive offer, no fathers or mothers were willing to hand over their children for the expedition. The only option was to recruit orphans, as there would be no adult claims for them. Children from the orphanage in Santiago de Compostela were therefore chosen. Balmis and Salvany calculated that the number of children needed to ensure the vaccine's safe arrival on American soil was a minimum of 22, which was the number of children finally enrolled in the expedition. These children, who soon became known at the *galleguiños*, were under the care of the orphanage's manager Isabel Cendales, a maternal figure for the children and the only woman on the expedition. The vaccination plan consisted of initially vaccinating two children. A week later, two more children would be vaccinated with the vaccine vesicles of the first, and so on. Two children were vaccinated in each round, to be sure that from at least one the vaccine could be transmitted.

The expedition sets sail from A Coruña

The corvette *Maria Pita*, captained by Pedro del Barco, was equipped for the expedition. Five hundred copies of Moreau de la Sarthe's book were loaded onboard for distribution to the vaccination boards, together with thermometers and barometers to confirm the efficacy of the vaccine in various weather conditions, thousands of glass plates to keep the vaccination liquid, and pneumatic machines to create a vacuum in the bottle containing the vaccination liquid. Loaded with this equipment and the aforementioned passengers, the *Maria Pita* set sail from the port of A Coruña on 30 November 1803 (Fig. 6). The first stop was the Canary Islands. In Santa Cruz, Tenerife,

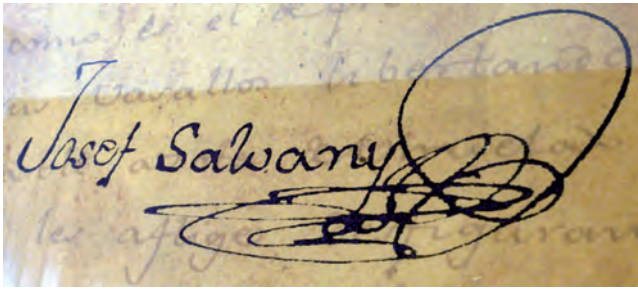


Fig. 5. Josep Salvany's signature.

there was a great welcome and the first vaccination board was set up successfully; from there, the vaccine could be sent to the neighboring islands.

Arrival in the Americas

The expedition's first contact with the Americas was in Puerto Rico, where its welcome contrasted sharply to that in Tenerife: absolute indifference, and even signs of hostility, reigned. The reason was that shortly before, the vaccine had arrived in Puerto Rico from the neighboring British colonies. Balmis and Salvany studied the procedures being followed and found flaws that endangered the success of the vaccination campaign. There were strong discussions with the Puerto Rican vaccinators and the *Maria Pita* departed without having fulfilled its mission on that island.

From San Juan, Puerto Rico, the expedition traveled next to Venezuela. The chosen port was La Guayra but a strong tropical storm, forced the expedition to disembark in Puerto Cabello. Here, the reception was once again triumphant and vaccines were received enthusiastically by the Venezuelans. The vaccination boards worked to perfection, allowing the campaign to spread throughout the country. From there, the hith-

erto single expedition was divided into two independent ones: Balmis directed the first, a maritime expedition, to Cuba, while Salvany directed the other, by land, to the rest of South America. As feared at the time of their appointments, despite being guided by the same spirit the junior and senior physicians never established a close working relationship. Another difference was in the degree of financial support. While Balmis still had at his disposal most of the money invested by the Court for the expedition, Salvany had a much more limited budget and was forced to seek his own funding.

Balmis' expedition to the north

The first stage of Balmis' expedition was Cuba. At Havana, everything was prepared for his reception and, as in Venezuela, the vaccination board functioned efficiently. However, while vaccination boards had been set up throughout the island, allowing for a massive vaccination campaign, there were no carrier children and no replacements. Thus, Balmis bought several black female slaves to serve as carriers for the vaccine until the next stop, the Mexican port of Sisal, in the Yucatan Peninsula. From there, sub-expeditions were organized, partly on land and partly by sea. The *Maria Pita* went to Veracruz, where the journey ended and the ship returned to Spain with the *galleguiños* and Isabel Cendales. In Mexico, the vaccination boards were also successful, allowing the vaccine to be extended across the territory and from there to the north, to the current American state of Texas, and to the south, to Guatemala and the rest of Central America. In the Port of Acapulco, Mexican children were recruited to continue with the vaccination campaign to the Philippines.

The Pacific journey was much more difficult than the Atlantic one because it was made on a mail ship that lacked the comforts of the *Maria Pita*. The children slept on the floor, where rats abounded, and the ship's movements caused some chil-



Fig. 6. Engraving of the departure of Royal Philanthropic Expedition of the Vaccines.

dren to be spontaneously infected by the vaccine, through mutual contact. Nonetheless, despite these hardships, the expedition reached the port of Manila, where it was also received with honors. Again, boards were set up to carry out massive vaccination campaigns, this time in all the Philippine islands. From Manila, the expedition, still directed by Balmis, went to the Portuguese enclave of Macau, on the Chinese coast, then continuing on to the Port of Canton, the entry point of the smallpox vaccine to China and the rest of Asia.

Understandably, Balmis was exhausted and decided to return to Spain on a Portuguese ship, sailing through the Indian Ocean, around the Cape of Good Hope and, in the Atlantic, once stopping at the small island of Santa Elena. At the occasion of his reception there, the English governor presented him with a package that he had received many years before, from Jenner himself, containing samples of the vaccine fluid and instructions for its application. Obviously, the fluid had already expired and was no longer usable. From Santa Elena, Balmis went on to Lisbon, where, in 1806, he had disembarked. Upon his return to Madrid, he was received with full honors by King Charles IV. Balmis died in Seville in 1819.

Salvany's expedition to the south

The expedition led by Salvany was of more precarious means, longer, and confronted with greater obstacles. Most of it was by land, but some stretches had to be undertaken by boat. The first stage was by sea, from the Venezuelan port of La Guaira to the Colombian port of Cartagena. It was along this route that the expedition suffered its first serious setback, running aground in the estuary of the Magdalena River. Luckily, the campaign could be continued by land.

Crossing the Colombian Andes into Ecuador was an authentic epic journey of heroism that did not dissuade the team from successfully completing its mission of vaccinating the maximum number of people. In Santa Fe, Salvany met with the botanist José Celestino Mutis, from whom he received abundant praise and encouragement to continue the expedition's meritorious humanitarian work. A very significant event took place in the Ecuadorian city of Cuenca. Simon Bolivar, who was fighting for Ecuador's independence, was aware of the vaccination campaign conducted by Salvany and asked the royalist authorities in Venezuela to provide him with the vaccine for his troops, who were suffering from a major epidemic of smallpox. Indeed, military hostility was set aside and the vaccine reached Simon Bolivar's soldiers.

Salvany's health had badly deteriorated. For many years he had suffered from diabetes and from malaria, which he probably contracted during his activity as a military health care worker in Extremadura. In America, he suffered from diphtheria and hemoptysis (TB), went blind in one eye, and one of his hands had to be amputated. Still, his spirits did not wane and he continued the vaccination campaign. In Lima, he even completed his studies and obtained a medical degree from the prestigious University of San Marcos. It was in the Peruvian capital that he became engaged in strong confrontations with several groups

of individuals who were marketing the vaccine, which challenged one of his fundamental principles: that preventive measures should be public, universal, and free.

Yet, Salvany still had the strength to organize new boards and promote sub-expeditions that extended throughout South America, all the way to Buenos Aires. He finally arrived in Bolivia where, exhausted, he died in the city of Cochabamba in 1810, at only 36 years of age. The words written several days before dying are especially moving,

"The lack of roads, the precipices, the large rivers, the deserted places we have encountered have not stopped us for even a moment, much less the waters, snows, hungers, and thirsts we have suffered. The rigors that the cruel contagion offered in our first steps served as stimulus to bring a brilliant purpose to noble and humanitarian tasks..."

It was 2 years later that Balmis became aware of Salvany's death.

Results of the expeditions

It is estimated that over a 1.5 million people were vaccinated during these expeditions— the first major worldwide campaign to carry out a preventive health measure. To reassure the various targeted populations that the vaccination was a preventive measure for healthy people, the boards were set up far away from hospitals, hospices, and homes, and were mostly located in schools and municipal establishments. The boards were also active in education, thus creating a network continue health education and assure continued training.

Unfortunately, the independence wars, which erupted during the final years of Salvany's expedition, led to the disbandment of most of the vaccination boards, hindering the desired continuity of the vaccination campaign. Nevertheless, it is clear that the enormous task undertaken by Balmis and Salvany was an important first step, one that contributed significantly to the World Health Organization officially declaring smallpox to be eradicated from the planet a little over a century and a half later.

Impact and dissemination of the vaccine expeditions

Great scientific personalities around the world have praised the achievements of these expeditions. Among them it is worth quoting Edward Jenner,

"I cannot imagine in the annals of History an example of philanthropy that is nobler and wider than this one."

and from Alexander von Humboldt,

"This voyage will remain the most memorable in the annals of History."

It is surprising, but achievements as extraordinary as the ones that have just been commented have so far had little impact in terms of public knowledge on either side of the Atlantic. The vast number of events in these expeditions would be more than appropriate for a multitude of literary, theatrical, film and televised works of all types of genre. The names of Balmis and Salvany should be featured in the central streets and squares in all major cities in Spain and Latin America, their memory should appear on coins, stamps, banknotes, etc. There is practically none of that. The only literary repercussions have been:

Theatre. *Venezuela consolada* (Venezuela comforted), a short play by the Venezuelan Andrés Bello, premiered in 1804, that honored Balmis' achievements.

Narrative. *Saving the World* by the American writer of Dominican origin, Julia Álvarez (2006); *Ángeles custodios* (Custodian angels) by Almudena Arteaga (2010); and *Los hijos del cielo* (The sons of heaven) by Luis Miguel Ariza (2010).

Poetry. *A la expedición española para propagar la vacuna en América bajo la dirección de D. Francisco Balmis* (To the Spanish expedition to spread the vaccine in America under the direction of D. Francisco Balmis), by Manuel Jose Quintana (1804).

We can anticipate that many more literary and popular science works publicizing the impact of these memorable expeditions will, over time, appear in all languages, thereby ensuring the continued appreciation of the two men and the many anonymous children who were critical to their success.