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The beginnings of smallpox vaccination in Spain seen through the correspondence of Ignacio María Ruiz de Luzuriaga (1801–1802)

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ABSTRACT

Edward Jenner's discovery of the smallpox vaccine spread rapidly across Europe. In Spain, vaccinations first took place in December 1800 and the practice flourished upon the private initiative of doctors, surgeons, state officials and members of the nobility in different parts of the country. Ignacio María Ruiz de Luzuriaga, secretary of the Royal Academy of Medicine of Madrid, is considered in medical historiography as a key figure of the introduction of the smallpox vaccine in Spain. Ruiz de Luzuriaga had a major role as a disseminator of the Jennerian technique and as a distributor of the vaccine fluid. Given his prestige as a doctor and his position in the Royal Academy, he was commissioned to establish a scientific and academic corpus on preventive measures to foster their understanding, uptake and good practice among Spanish vaccinators. He also attempted to create a Central Vaccine Committee, such as that existing in other European countries. The Royal Academy kept records of his activity which have been filed and catalogued in a documentary set entitled 'Papeles sobre la vacuna' [Vaccine Papers]. This archive has not been studied in depth to date. These documents allow identifying a network of correspondents set up by Ruiz de Luzuriaga. He provided these correspondents with the vaccine and asked them to report back on the vaccination progress made in their municipalities. This correspondence provides an account of how the first immunisations in Spain unravelled, as well as of the initial concerns that accompanied the introduction of the vaccine.

1. The propagation of an idea

Throughout the eighteenth century, smallpox reached a peak of devastation. In its wandering as a world scourge, the disease decimated the population indistinctly across social classes, leading to significant changes in the future of European monarchies [1].

The implementation of variolation had created a favourable climate for the possible prevention of the disease. The technique consisted in transferring fluid from the pustules of a smallpox patient to a healthy subject, producing immunity to the disease if it was carried out under the right conditions.

Variolation was a new field of knowledge, it paved the way for the subsequent introduction of the smallpox vaccine [2]. The vaccine's discovery shook nineteenth-century medical practice. It was variant of the practice of inoculation, and was based on the empirical observation that people infected with the variolose disease that developed in cows (cowpox), became resistant to human smallpox (smallpox). The method was described and rationalised by the English surgeon Edward Jenner (1749–1823), an exponent of the Enlightenment, who studied diseases based on systematic observation and experimentation [2,3].

On 21 June 1798, Jenner sent his work *An inquiry into the causes and effects of the variolae vaccine...* [4], to press, that would produce a decisive turnaround in the fight against smallpox. The text exposed an empirical model that was the forerunner of the science of vaccinology [5] it was translated immediately into several languages and the Jennerian vaccine spread at an unusual speed across main European cities between 1799 and 1800 [6–13].

However, this apparently successful spread of the vaccine was also accompanied by controversy. Difficulties emerged relating to social acceptance, to technical issues regarding the administration of the vaccine, its protective efficacy, and to problems in the transport of the vaccine fluid. These concerns created a division between vaccine enthusiasts, who demanded greater legislative support, and detractors whose arguments referred to a possible lack of safety or potential adverse effects [14].

France was Spain's gateway for enlightened European knowledge of the time. News of Jenner's discovery and the supply of the necessary fluid to carry out the first vaccinations came via

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France's territory. Specifically, on 3 December 1800, in the town of Puigcerdá (Catalonia), Doctor Francisco Piguillem y Verdaguer (1770–1826), member of the Royal Medical Academy of Barcelona, inoculated four children with the vaccine. The fluid had been sent from Paris by François Colon, only four months after the latter had performed a vaccination for the first time in the French capital.

Piguillem had set the example and he was followed by various vaccinators who were also connected to academies or medical institutions. Various geographical points of vaccine dissemination in Spain could be identified, such as the Basque-Navarrese region or Madrid [14]. In this latter city, the vaccine's greatest proponent was Ignacio María Ruiz de Luzuriaga (1763–1822), a doctor and secretary of the Royal Academy of Medicine of Madrid, who launched the practice of vaccination in the capital on 22 May 1801 [14,15].

For two years, Ruiz de Luzuriaga, from his position at the Academy, led an intensive epistolary activity, corresponding with people interested in the vaccine. Thus, a national network of correspondents was formed, requesting not only vaccination fluid but also instructions on how to administer it. Ruiz de Luzuriaga provided them with vaccine and knowledge about the technique, and in return requested information on their progress and experiences: he could thus obtain first-hand reports on the safety and efficacy of vaccinations. This correspondence constitutes an excellent documentary source to understand some of the circumstances that underlied Spain's first vaccinations. We have been able to identify the numerous correspondents, as well as their occupation and social class, their geographical location, their interests, concerns and initiatives related to vaccination [16].

2. Ruiz de Luzuriaga and Smallpox

Considered in medical historiography as one of Spanish medicine's key figures under the Enlightenment. Ruiz de Luzuriaga, addressed multiple aspects related to hygiene, public health and medical-social problems [17,18].

His scientific interests included the introduction of the smallpox vaccine in Spain, and he assumed a prominent role as an ardent advocate of the vaccine and disseminator of the Jennerian technique [19].

Ruiz de Luzuriaga was born in Villaró (Vizcaya) on 31 July 1763. His father, José Santiago Ruiz de Luzuriaga, was a physician and member of the Sociedad Bascongada de Amigos del País [Basque Society of Friends of the Country], an institution that promoted variolisation and in which it distinguished itself as an inoculator since 1770, as reported by Timotheo O'Scanlan (1726–1795) the best known promoter of inoculation in Spain [20].

Thus, from a young age, Ruiz de Luzuriaga became acquainted with inoculation through his father, and broadened his knowledge during his medical and chemical education in Paris, London and Edinburgh, after which he returned to Spain. Based in Madrid, he joined the Royal Academy of Medicine in Madrid in April 1790, in which he held various positions.

Given this positive prior experience of inoculation, together with an excellent education and access to the most relevant scientific knowledge of his time, it is unsurprising that Ruiz de Luzuriaga became actively committed to vaccination [18].

3. Correspondence on the vaccine

Between 1801 and 1802, three occurrences led Ruiz de Luzuriaga to dedicate himself to the vaccine, beyond his activity as a vaccinator at his home in Madrid. First, a letter from the Vaccine Commission of the Paris Medicine Society was sent in June 1801 to the Academy requesting information on the status of the vaccine in Spain; second, he was pressured by the royal chamber physician Ignacio Jáuregui and officials of the Secretary of State to write a monograph on the vaccine that would serve as a reference; and, finally, he was mandated by the Protomedicato Tribunal to report on everything relating to vaccination [19].

By accepting these commitments, Ruiz de Luzuriaga became a key player during the first period of dissemination of the Jenner method in Spain [15]. Numerous correspondents went to him to obtain the vaccine and instructions on its use; in exchange, the Secretary of the Academy received information on the outcome of the operations carried out [15].

Ruiz de Luzuriaga kept the results of these epistolary contacts together with some of his own writings in a series of folders, named '*Papeles sobre la vacuna*', [Vaccine Papers], which are part of the documentary collection of the Royal Academy of Medicine of Madrid (RANM). There are four volumes, each individually signed [19]. The first three contain letters addressed to Ruiz de Luzuriaga by people interested in the vaccine (Tables 1, 2, 3).

To date, this correspondence has not been examined in depth. One study chronologically related a significant, yet not exhaustive part of the correspondence [21], four other publications have analyzed some letters [15,18,22,23], according to the sender.

The total number of letters contained in the first three volumes amounts to 149. It was not possible to identify the sender's occupation in 15 of them (Table 3), and 7 letters were written by Ruiz de Luzuriaga himself (Table 1); (Table 2). Of the remaining 127 letters, 105 (82.7%) were addressed to Ruiz de Luzuriaga, the others were addressed to a third party. Its authors were mostly aristocrats, senior state officials and health professionals (doctors and surgeons).

The total number of well identified senders is 65. The majority of correspondence corresponds to 1801, (90.3%, n = 130) and are mostly dated during the months of August, September and October. Identifying the rest of the letters in 1802.

The topics addressed in the letters concern first and foremost favourable predispositions and adherence to vaccination [75.2% (n = 112)], followed by results on the number of people vaccinated [60.4% (n = 90)]. Controversy or doubt as to the vaccine's efficacy and its possible adverse effects was a subject present in 29.5% (n = 44) of the messages. To finish, a total of 23.5% (n = 35) and 19.5% (n = 29) of the letters respectively requested vaccine fluid or instructions on administration techniques.

The correspondence falls into two categories, according to the professional and social category of its senders: letters written by members of the aristocracy, bourgeoisie and state officials; and that composed by professional colleagues, i.e. doctors, surgeons and bleeders (Table 1).

4. The role of the aristocracy and senior state officials

The professional prestige of Ruiz de Luzuriaga is visible through the contacts analyzed in the identified correspondence, including the letters written by the secretary himself. A total of 30.6% (n = 41/134) of senders corresponded to palace aristocracy, nobility and senior state officials, all showing favourable attitudes towards the vaccine.

Their constant requests for information on the new Jenner method and the example they gave by exposing their own children to the supposed benefits of vaccination fulfilled a moralising and pedagogical function that encouraged the rest of the population to get vaccinated.

A total of 41 letters are included in this group, geographically distributed as follows: Madrid (16), Soria (7), Bilbao (4), Guipúzcoa (3), Burgos (3), Zaragoza (2), Badajoz (2), Jerez de los Caballeros (2), Vitoria (1) and Murcia (1) (Table 1).

Table 1
Correspondence found in the 'Vaccine Papers' according to occupation (State civil servants, Aristocracy and Enlightened Bourgeoisie) and municipality.

State civil servants, Aristocracy and Enlightened Bourgeoisie	Letters (41)	Sent to Luzuriaga (32)	Not sent to Luzuriaga (5)	Letters send by Luzuriaga to (4)	Occupation	Municipality	**Volume**
Conde de Isla	1	–	–	1	Noble	Madrid	1*
Condesa de Montijo	2	1	–	1	Noble	Zaragoza	1*
Dámaso de la Torre	1	1	–		Secretary of State	Madrid	1*
Evaristo Pérez Castro	2	–	2		Secretary of State	Jerez Caballeros	1*
Feliciana Matute	1	1	–		Merchant	Madrid	1*
Juana Villachica y Laguna	3	3	–		Noble	Burgos	1*
Lope de Mazarredo	4	3	1		Noble	Bilbao	1*
Louis Proust (Don Luis)	1	–	–	1	Chemist	Madrid	3*
Luis de Onís	2	1	–	1	Civil Servant	Madrid	1*
Luis Quadrado	1	1	–		Lawyer	Murcia	1*
Manuel de Albuerne	1	1	–		Treasury Secretary	Madrid	1*
Manuel de Ascargorta	1	1	–		Noble	Madrid	1*
Martín García de Olalla	1	1	–		Merchant	Madrid	1*
Marqués Narros	1	1	–		Noble	Vitoria	1*
Marquesa de Monsalud	2	2	–		Noble	Badajoz	2*
Marqueses de Vadillo	7	6	1		Noble	Soria	1*
Nicasia Pérez de Castro	2	2	–		Noble	Madrid	1*
Paula Bordó	1	–	1		Merchant	Madrid	1*
Pedro Morales Pastor	1	1	–		Lawyer	Madrid	1*
Vicente González Arnao	1	1	–		Lawyer/Writer	Madrid	1*
Xaviera de Muzgategui	3	3	–		Noble	Guipúzcoa	1*
Zamacola	2	2	–		Noble	Madrid	2*

1* RANM, *Papeles sobre la vacuna*, Signatura 17-2ª S. gobierno, 18, fols. 1-386.
2* RANM, *Papeles sobre la vacuna*, Signatura 17-2ª S. gobierno, 19, fols. 1-255.
3* RANM, *Papeles sobre la Vacuna* 1802, 23-4ª Biblioteca, fols. 1-527.

Table 2
Correspondence found in the 'Vaccine Papers' according to occupation (Health professionals) and municipality.

Health professionals	Letters (73)	Sent to Luzuriaga (68)	Not sent to Luzuriaga (3)	Letters send by Luzuriaga to (2)	Occupation	Municipality	**Volume**
Antonio Franseri	3	2	–	1	Doctor /Academy	Madrid	1* 2*
Antonio Goñi	1	1	–		Surgeon	Asturias	1*
Félix Martínez López	4	4	–		Doctor	Valladolid	1* 2*
Francisco Balmis	1	1	–		Doctor	Madrid	2*
Francisco de Neyra	1	1	–		Doctor /Academy	Madrid	1*
Ginés Lario	1	1	–		Doctor	Madrid	3*
Ignacio Aguas-Vivas	2	2	–		Doctor	Alicante	1*
Ignacio Jáuregui	23	23	–		Doctor	Madrid	1*
Isidro Scardini	4	2	1	1	Doctor	Madrid	1*
José Ubis	4	4	–		Surgeon	Soria	1* 2* 3*
Juan Antonio de Ugalde	4	4	–		Surgeon	Bilbao	2*
Juan Bautista Soldevilla	1	1	–		Doctor /Academy	Barcelona	1*
Juan de Azaola	1	1	–		Surgeon	Madrid	1*
Juan Manuel de Aréjula	4	3	1		Doctor/ Academy	Cádiz	1*
Lucas Dueñas	1	1	–		Surgeon	Valladolid	2*
Manuel Gorgullo	1	1	–		Doctor	Madrid	1*
Nicolás de Cortázar	1	1	–		Bleeder	Madrid	2*
Pascual Quartero	1	1	–		Surgeon	Cuenca	3*
Pedro Fernández Acevedo	1	1	–		Surgeon	Madrid	1*
Prudencio Valderrama	8	8	–		Doctor	Burgos	1* 2*
Tomás Carpio	1	–	1		Surgeon	Tudela	1*
Vicente Martínez	3	3	–		Doctor	Pamplona	1*
Vicente Mitjavila	2	2	–		Doctor	Barcelona	2* 3*
Foreign health professionals	Letters (20)	Sent to Luzuriaga (5)	Not sent to Luzuriaga (15)	Letters send by Luzuriaga to (-)	Occupation	Municipality	**volume**
Paris Commission Vaccine	11	3	8	–	Doctors	Paris	1* 2*
Alfonso Leroy	6	–	6	–	Doctor	Paris	1*, 2*
Joao Francisco de Oliveira	2	1	1	–	Doctor	Lisbon	2*
Tomas Romay	1	1	–	–	Doctor	Havana	2*

1* RANM, *Papeles sobre la vacuna*, Signatura 17-2ª S. gobierno, 18, fols. 1-386.
2* RANM, *Papeles sobre la vacuna*, Signatura 17-2ª S. gobierno, 19, fols. 1-255.
3* RANM, *Papeles sobre la Vacuna* 1802, 23-4ª Biblioteca, fols. 1-527.

Contents of the letters follow two series of interests. First, they expose their curiosity and positive reactions regarding Jenner's discovery. They requested technical information on the vaccination by writing directly to Ruiz de Luzuriaga or by writing to a family member residing in Madrid, who would then transfer the letter to Luzuriaga. These first contacts took place during the months of July and August 1801, as early as two months following Ruiz de Luzuriaga's first vaccinations in Madrid.

Table 3
The correspondence found in the "Vaccine Papers" whose occupation or municipality of the sender was not identified.

	Letters (15)	Sent to Luzuriaga (13)	Not sent to Luzuriaga (2)	Occupation	Municipality	Volume
A.P.O	1	–	1			2*
Antonio Cano	1	1	–		Córdoba	2*
Ignacio Gadea	1	1	–		Guadalajara	2*
Joaquín Rosello y Larraondo	1	1	–		Madrid	2*
José Fernández de Pinedo	1	1	–		Madrid	1*
Juan Andújar	1	1	–		Jaén	1*
Juan González Castañar	1	1	–		Cádiz	1*
Manuel Abad	1	1	–		Madrid	1*
Manuel Álvarez Terrero	1	1	–		Álava	3*
María Juana de Garralde	1	1	–		S. Sebastián	2*
Micaela de Gavira	1	–	1		Madrid	1*
Sr. Amorós	1	1	–		Valencia	1*
Sr. García	1	1	–		Madrid	1*
Sr. Omaña	1	1	–			1*
Sr. Robles	1	1	–			1*

1* RANM, Papeles sobre la Vacuna. Signatura 17-2ª S. Gobierno, 18 fols. 1-386.
2* RANM, Papeles sobre la Vacuna. Signatura 17-2ª S. Gobierno, 19 fols. 1.255.
3* RANM, Papeles sobre la Vacuna 1802, 23-4ª Biblioteca fols. 1.527.

For example, Doña Juana Manuela Villachica y Llaguno (1774–1812), the wife of Francisco Enrique de Urquijo, a future mayor of Burgos appointed by the king during the French occupation, sent an intimate letter to Ruiz de Luzuriaga on 29 July 1801 from Burgos:

> "I beg you to give me your opinion and that of the other doctors on vaccine inoculation, which we have heard of here. We have pondered the method's benefits. My husband's family has been cruelly stricken with smallpox, and he himself has just suffered the disease, (...) there have been many serious cases; after having put his life at risk, he has been left extremely affected, although thanks to God, he has suffered no eye injury or any imperfection; two sisters have yet to catch the disease, (...) we would like to spare them the danger of such an epidemic, and therefore we await your opinion, as well as a description of the method to follow in the event of undertaking the inoculation; we have a good doctor, but he does not dare to proceed as he dos not dispose of the fluid to be introduced and is not fully aware of this new way of inoculating" [22].

At a second stage, once instructions had been received, letters focused on the results and progress of the vaccinations. This information was provided by doctors or surgeons linked to the municipality or the service of the family in question, and who took over the correspondence with Ruiz de Luzuriaga.

In Burgos, Juana María Villachica, told Luzuriaga (9 August 1801) that she received the vaccine he sent her, and that it was doctor Prudencio Valderrama who performed the operations on his own daughters, 'so the example be an encouragement to others'. Valderrama sent 'the result of the vaccination performed for the first time in this city, on my two daughters' to the Secretary of the Academy on 29 August" [22].

Similar data were provided by González Castejón, Marqués de Vadillo, and the Soria doctor Josef Ubis. The figure of the Marqués de Vadillo was highlighted by the health professional, who referred to him as a promoter of the vaccine on Sorian lands and neighboring Navarra, "the pus has spread in all the vicinity (...). The villages where cattle have been sent are Pamplona, Berlanga, Santa Cecilia and Tudela" [23].

5. Correspondence with other health professionals

The bulk of the correspondence was written by people connected to the field of health. We found that a total of 93 letters (69.4%) were sent by doctors, surgeons and bleeders, both from inside the country (73 letters) and from abroad: Paris (17), Lisbon (2) and Havana (1) (Table 2).

On the whole, the contents of this correspondence highlight the technical aspects of the vaccine and how to acquire it, the instructions to carry out the operation and how to communicate its results. This latter question was at the request of Ruiz de Luzuriaga.

A large number of health professionals requested the vaccine, some of them members of the Academy, others linked to the university and even the future Director of the Royal Vaccine Expedition (1803–1813), Francisco Javier Balmis and Berenguer. (1753–1819) (Table 1).

Ignacio Jáuregui, the royal chamber physician, stands out among the health professionals appearing in Ruiz de Luzuriaga's correspondence. He played a major role, not only for the sheer volume of his correspondence, but also because of the significant part he played in introducing the vaccine into the courtly circles of the kingdom's capital. Jaúregui, in addition to introducing the vaccine in Aranjuez, transmitted the government's interest in knowing everything relating to vaccination to Ruiz de Luzuriaga, encouraging him to prepare different reports on the progress of the vaccine in Spain and to write a review of the state of the art to clarify the procedure and solve any methodological questions.

6. Map of correspondents

When examining the geographic distribution of all correspondence with a municipality identified in Spain, several centres can be considered as active disseminators of vaccination (Fig. 1).

In addition to Ruiz de Luzuriaga's surrounding environment, that is, Madrid and the Court (Aranjuez), that represent a total of 58 letters, including those of Jáuregui (23), the remaining correspondence that identifies the municipality of the sender from the interior of the country (68) reveals an axis going towards the north of the peninsula.

A total of 27 letters were sent from today's Community of Castile and Leon; they relate the first vaccinations to take place in the provinces of Soria, Burgos and Valladolid. The letters sent from the Basque Country (14) and Navarre (4), enable to identify another geographical concentration coinciding with Ruiz de Luzuriaga's hometown and personal relationships. Moreover, this territory is close to France, an influential passage way for the penetration of new ideas and a key country for scientific education [24]. The Real Sociedad Bascongada de Amigos del País organised study trips to the neighbouring country to acquire knowledge and training to then apply locally. Among the young Basques who underwent

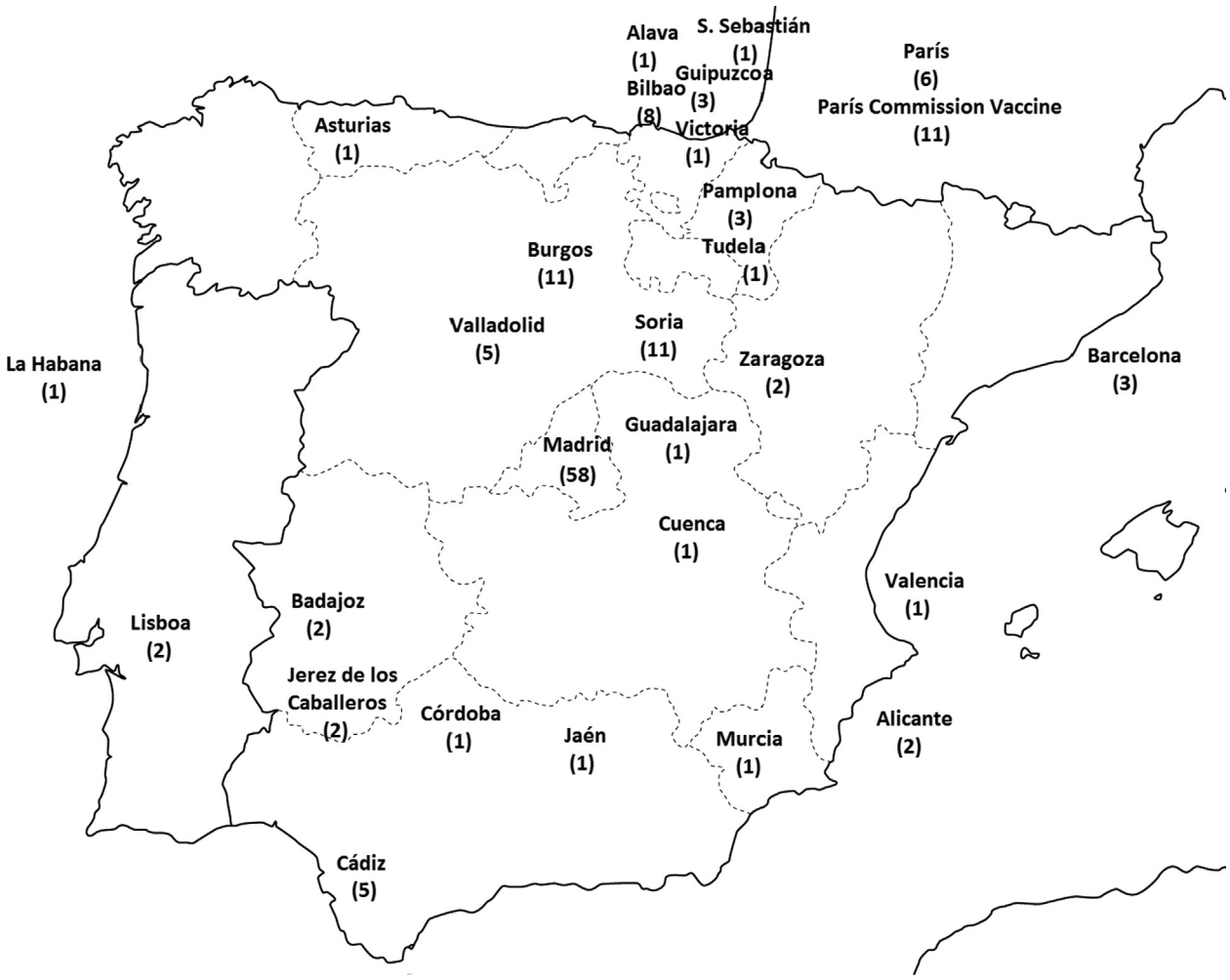

Fig. 1. Geographical distribution of the correspondence contained in the "Vaccines papers" 1801–1802.

apprenticeships abroad were Ruiz de Luzuriaga, Ramón María Munibe, son of the Count of Peñaflorida and Javier Eguía, son of the Marquis of Narros [25]. All of them were members of the wealthiest enlightened classes.

A total of 8 letters were sent to Ruiz de Luzuriaga from Bilbao by Lope García de Mazarredo, doctor and city councillor, and by the surgeon Antonio de Ugalde. The correspondence shows the vaccine had been well received by society in Bilbao and, above all, it reveals Lope García de Mazarredo's intense pro-vaccine activity.

The Navarre area, where correspondence was emitted from Pamplona (3) and Tudela (1), was another vaccine dissemination centre. Writings from Pamplona were sent by Vicente Martínez, a 'Doctor who served the Royal Armies, and presently serves the General Hospital of the city of Pamplona'. In 1802, he published a '*Historical Practical Treatise on the vaccine*' [26]. In this work, he emphasised how important it was that influential personalities in society give an example by vaccinating their own children to help disseminate the vaccine.

Finally, Andalusia was identified as another location where the vaccine was administered and spread early, though the volume of correspondence is less significant. The total number of preserved letters amounts to 7, of which 5 come from Cádiz and 2 from Córdoba and Jaén.

The letters were not limited only to Spain, they were also remitted from Paris, Lisbon and Havana (Fig. 1). From Cuba, the physician and provaccinator Tomás Romay Chacón (1764–1849) [27], wrote (19 April 1802) to Ruiz de Luzuriaga to thank him for his mediation in being appointed as Correspondent Member of the Royal Academy of Medicine of Madrid. He goes on to describe his work as introducer and disseminator of the vaccine on the island, "I am currently reprinting a booklet printed at Court translated from French by Dr. Pedro Hernández on the origins and uses of the vaccine" [28]. He was referring to a text "Origen y descubrimiento de la vaccine" published in 1801, by the physician Pedro Hernández that had been widely circulated [29]. The location of the vaccination fluid became one the vaccinators' concerns at the time, out of fear of its depletion. Romay communicated this to Ruiz de Luzuriaga, conveying that "I have hopes of obtaining it on this Island, because an inhabitant of an inland village, where a lot of cattle are raised, assures me that he has observed the pimples on cows, and they used to be caught by those who milked them; but he did not notice or know whether these people had been stricken with smallpox" [29].

His expectations were to be mitigated years later, as an agreement was settled between the Royal Economic Society of Havana and the Economic Council of the Royal Consulate, to award a prize of three hundred pesos 'to whoever would bring the cow virus from other countries and four hundred pesos to whoever discovered it in our cows'. Although the owners of the haciendas referred to the presence of cowpox in the cows of the region, nobody claimed the prize, as indicated by Romay [30].

In Paris, two entities semi-official were established to follow up the progress of the vaccine, after the early interest in vaccination. On the one hand, the Comité Central de la Vaccine [Central Vaccine

Comittee], was created in February 1800 as a subscriber society. A year later, *Commission de Vaccine séante au Louvre* [Louvre Vaccine Comission] was established under the aegis of the Society of Medicine [19]. A total of 11 documents included in the 'Papeles sobre la vacuna' come from the latter institution, dated between 23 June and 16 November 1801. In these letters, information was requested on the status of the vaccine in Spain, when vaccinations are started, who had been the supplier of the cow fluid, its dissemination, the population's degree of acceptance and the existence of detractors. They also attached the first report on the vaccine that this Society had prepared [31], promising to send a second [32,19]. This reflected a desire to exchange knowledge and maintain good relations between academic institutions. These reports were signed by its president Jean Sédillot (1757–1840) and by the secretary Jean-Baptiste Emonnot (1761–1823) [32].

We identified 6 texts transcribed by Ruiz de Luzuriaga that correspond to letters published in the newspaper La Clef du Cabinet des Souverains (1801) by Alphonse Leroy (1742–1816), a professor of Obstetrics at the École of Medecine in Paris and a notable enemy of vaccination:

> "I see with pain that this fatal gift has been received with enthusiasm out of fashion, and that the doctors have adopted it with a certain kind of enthusiasm, while my confrères, who, like me, have thirty-five years of experience and observation (...), are today contrary to this practice, even when smallpox is foreseen, which is not the case" [33].

Finally, two texts by Joao Francisco de Oliveira, Portugal's royal doctor, dated in March and sent from Queluz Palace, requested information from Ruiz de Luzuriaga on the vaccine against a smallpox outbreak that was taking place at the Portuguese court. Oliveira expressed his lack of experience on the subject and needed to advise the Prince Regent on the actions to follow [34]. This request confirms Ruiz de Luzuriaga's good scientific reputation outside Spain.

7. Controversies on the vaccine

The smallpox vaccine was controversial since its inception, as its efficacy and safety were put into question. This debate arose in all countries as they adopted the method. Many publications at the time show the efforts undertaken by vaccine advocates to explain the procedure's good practices and how to minimise possible adverse effects. The debate on vaccine effectiveness and safety continues today, even given the much more stringent oversight. A crisis of confidence in vaccine efficacy and safety has emerged across the globe, named "vaccine hesitancy", as people have forgotten the severity of these diseases, which have either been eradicated (globally or regionally) or occur relatively infrequently. This has become a topic of research [35].

The correspondence examined in this study equally reflects this question.

Following the administration of the vaccine, Ruiz de Luzuriaga entered in discussions about its lack of effectiveness or the appearance of adverse effects. He was even criticised. His friend and colleague Ignacio Jáuregui, who had also been criticised on several occasions, told him in a letter written in August 1801: 'My friend, I have equally been disturbed here [Aranjuez] because of an imposture, as you have there [Madrid] by Scardini" [36]. He was referring to an undesired effect of the disease of smallpox after being vaccinated a girl, niece of the doctor Isidro Scardini that he had aired in the press. Although the vaccine was administered by surgeon Francisco Leyral, Ruiz de Luzuriaga and other doctors from the Academy examined the case and concluded that the girl had suffered from chickenpox.

Opponents of the vaccine resorted to publicising these failures to discredit the method. The periodical press disclosed the most striking failures, especially when children of notable personalities in society were involved.

The death of the son of Count of Castro Terreño, in September 1801, was among the vaccine-related events to have the biggest adverse impact on public opinion; it was one of the occurrences that Ruiz de Luzuriaga had to give most explanations about in his correspondence. The child had died a week after being vaccinated by Juan Azaola, a surgeon at the Hospital of Madrid and a collaborator of Ruiz de Luzuriaga. The news was widely circulated.

Several letters sent between September and December, both by health professionals and aristocrats, requested clarification from Ruiz de Luzuriaga on the case to simply dispel their doubts as they maintained a favourable disposition towards the vaccine. For example, the Countess of Montijo wrote on 12 September from Zaragoza, "I have not hesitated to place my trust in you, knowing your love for humanity, and your eagerness to spread this good everywhere, the death of the child of Castroterreño somewhat worried me, but I do not think it is the effect of vaccination' [37].

The truth is that Ruiz de Luzuriaga could not clarify the event, in fact, associated the death of the nobleman to statistics and high infant mortality at the time, as stated in his impartial report, "if in all countries the two thirds die parts of children born before the age of 2 years, as it results from the obituaries, which should not happen in a court, where hereditary bad moods are so common, where scrofulous and rachitic vices dominate the first of which aggravates the pox" [38].

The event endangered the continuation of vaccinations, but was overcome thanks to the help of the nobles who continued their vaccinations and thus motivated the rest of the population. "Perhaps it [the vaccination] would have totally declined had His Excellency the Prince of Peace not have immediately and fortunately vaccinated his only daughter, and his niece, daughter of the Marquis of Branchiforte. Thanks to this laudable example, more than 85 people were vaccinated in my house the next day. Let it be known that the Marquess Widow of Villamejor, despite having been informed of the fatal event, presented herself to be vaccinated at 50 years of age" [15,39].

Opponents to the vaccine included some doctors who did not trust their prophylactic properties or had more personal interests. Diego de Bances, introducer of the vaccine in Navarre, summed it up in 1802: "There has been no lack of teachers, who either to distinguish themselves, or for more vile and interested purposes, have fostered doubt and distrust on the harmlessness of the vaccine disease and on its virtue in protecting agains smallpox. Fortunately, the greatest number of anti-vaccinators have been inoculators by trade, or who run inoculation houses in France. As the discovery harms their establishments, and suppresses the greatest support to their existence, they have cried out against good that brings them so much evil" [40].

8. Final considerations

The analysis of the correspondence, sparsely studied so far, reveals little support by the Spanish government authorities during the initial stage in the spread of smallpox vaccine. An institutional support necessary to establish a centralized and methodical model for the propagation of the vaccine fluid, through the creation of a Central Commission of the vaccine, as, for example, in France or England, that guaranteed a more effective control and less spontaneous practice of vaccination.

Ignacio María Ruiz de Luzuriaga was obliged by the circumstances to take on a leading role in the introduction of the vaccine against smallpox. He was a prestigious doctor, well connected

abroad and held the position of Secretary at the Royal Academy of Medicine in Madrid. He was thus considered as a figure of reference by both government authorities and colleagues.

He was asked by the government to respond to requests from foreign institutions (the Paris Vaccine Commission located in the Louvre) and national institutions (the Real Protomedicato), so he had to write a range of reports [38]. Faced with the need to gather information to prepare them, he performed a twofold task, seeking the collaboration of colleagues and responding to spontaneous vaccine requests from different parts of the country. Thanks to the network of correspondents that he successfully established, he was able to detect progress made in vaccinations as well as to weigh the opinions and concerns about the vaccine that were transmitted to him.

The correspondence shows the rapid spread of the vaccine in the peninsula, reveals the enthusiasm of the more enlightened classes to adopt the method against a certain indifference of the disadvantaged classes, more given to distrust, no doubt, motivated by the difficulties to access information and knowledge. The letters also indicate the adherence of a large number of health professionals (doctors and surgeons), open minded, who accepted the commitment to propagate and promote the continuity of the new practice, evidencing a paradigmatic sample of knowledge transfer between the different social classes.

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Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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