

**WHAT EVIDENCE FOR A CHOLERA VACCINE?
JAIME FERRÁN'S SUBMISSIONS TO THE PRIX BRÉANT**

Clara Uzcanga, Universidad Nacional de Educación a Distancia, Madrid, Spain

David Teira, Universidad Nacional de Educación a Distancia, Madrid, Spain

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ABSTRACT

This article analyses how the French Academy of Sciences assessed Jaime Ferrán's cholera vaccine submitted for the Prix Bréant in the 1880s. Ferrán, a Spanish independent physician, discovered the treatment in 1884 and tried it on thousands of patients during the cholera outbreak in Valencia the following year. His evaluation sparked a controversy in Spain and abroad on the vaccine's efficacy. The Bréant jury did not see any evidence for it in Ferrán's submission, a decision usually interpreted in terms of French scientific nationalism (or simple chauvinism): an outsider from the scientific periphery could not be awarded the Bréant. Drawing on the archival records of the award, we suggest that Ferrán failed instead to provide data that the Academy could consider unbiased, according to the contemporary standards for data presentation. We will illustrate these standards at work in the assessment of another submission from Spain, by Philipp Hauser, who received the Bréant for the thoroughness of his statistical endeavour.

Keywords: Ferrán, cholera, vaccine, data, Bréant, Académie des Sciences.

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1. The history of a failed cholera vaccine

The evaluation of new medical treatments is always potentially controversial. The different stakeholders involved (patients, physicians, manufacturers, etc.) often have conflicting expectations about the therapy. If the evaluation contradicts any of these prior expectations, the controversy about its methodology could be endless. Before the

emergence of the current consensus on the randomized clinical trial as the ultimate benchmark for therapeutic innovations, such methodological controversies proliferated. We are going to study one of these debates that started among physicians assessing a vaccine by the end of the nineteenth century, and then morphed into a debate among historians of the episode in the twentieth century.¹

Jaime Ferrán (1852-1929) was a Spanish physician and a pioneer of bacteriology who features in the history of cholera research for his purported discovery of a vaccine for the disease in 1884.² He tried it on thousands of patients during the outbreak in Valencia the following year. International scholarship considers Ferrán a pioneer in cholera vaccination, remaining generally agnostic about his self-proclaimed success.³ Spanish historians of the controversy are often more positive about the efficacy of the vaccine, even suggesting that Ferrán was denied the early international recognition he would have deserved just because he was an outsider from the European periphery, without any political or scientific influence in Paris.⁴

These two historiographical approaches (positive and agnostic) can be traced back to the initial reception of Ferrán's vaccine. As soon as the vaccination campaign started, several Spanish and foreign delegates came to Valencia to document the process and the evaluation of the vaccine's efficiency. The response was contradictory: while many argued that the evaluation was inconclusive, others found it effective and requested official support for Ferrán to develop the compound, although their efforts proved to be unsuccessful. Perhaps to settle the controversy and have his authority acknowledged, Ferrán made a series of submissions in the 1880s to the Prix Bréant, a generously endowed award of the French Academy of Sciences incentivizing progress in cholera research.⁵ His two initial attempts failed in 1885 and 1886, but two decades later, in 1907, the Academy would finally award Ferrán a Prix Bréant for his life achievements (although remaining agnostic about the efficacy of his vaccine). This distinction arrived too late for Ferrán and his supporters, who had already accused the Academy of sheer chauvinism in 1885. This accusation was later progressively incorporated into the historiography of the controversy, becoming a narrative about scientific nationalism in Europe at the end of the nineteenth century.

According to the *Ferranistas*, the Bréant jury was deliberately neglecting the evidence Ferrán had provided due to his nationality. Our goal in this paper is to provide an alternative account of the Academy's decision, in which *the way Ferrán presented his*

data becomes instead the key factor to explain the dismissal of his submissions. After examining the Academy archives, we argue that there is not enough evidence to support the claim of chauvinism. Instead, the archives indicate that the problem rested in the presentation of the data: Ferrán's reviewer struggled to make sense of the data he had submitted, composed of simple lists of figures without a unified presentation template and no systematic analysis.

Historians of medical statistics have focused mostly on the development of statistical methods to grasp a vaccine's efficacy, a process in which Daniel Bernoulli's analysis of smallpox inoculation and Karl Pearson's report on enteric fever inoculation are clear landmarks. Neither Ferrán nor his reviewers at the Academy used any sophisticated statistical technique in their assessments. This is far from surprising since, throughout the nineteenth century, quantitative techniques were not popular among the Parisian medical establishment, and they were almost unknown in Spain.⁶ However, the assessment of statistical data by the Bréant jury in the 1880s seems to be an episode of a different process: the growing relevance of data presentation formats as an element of proof in medicine.

Tabulation seems to have been the format of choice for data curation in nineteenth-century public health systems. By the end of the eighteenth century, James Jurin was arguing about how to properly tabulate mortality data to provide evidence for the efficacy of variolation. In the following decades, mortality tables inspired the development of a number of proto-epidemiological concepts. As we will see below, blank forms became a crucial tool in cholera research, thanks to the hygienist approach initiated by Max von Pettenkofer (1818-1901) in the 1850s. At the same time, according to V. Hess, during the nineteenth century the Parisian medical community was adopting standardized clinical records at hospitals for medical and administrative purposes.⁷ This is still a history under construction, and we cannot tell yet whether the Bréant jury shared a consensual standard for evidence presentation, be it in the form of tables or any other classificatory device. But the two Bréant submissions we discuss in this paper suggest that the Academy of Science was sensitive about data presentation as an element of proof.

As Ulrich Tröhler has argued, since the eighteenth century there had been a growing awareness among physicians, first in Britain and then in other parts of Europe, about the necessity of fair comparison for evaluating medical treatments.⁸ A comparison would be fair if the treatment offered controls for all the relevant causal factors in the

different groups of patients under study, so that if patients improved, their recovery would be due to the treatment and not to any uncontrolled confounder -what we would now call a *bias*. The early evaluations of variolation illustrate how tabulation allowed an experimenter's audience to inspect what variables had been controlled for (age, gender, etc) and whether there was any bias in the comparison.

We argue that the Academy shared an increasing concern with the way in which clinical observations were processed as an index of the quality of the evaluation, independently of the hypothesis under analysis. Against a widespread account of Ferrán's failure, we want to show that the jury's assessment of Ferrán's evidence was mediated by something else than national interests: a methodological concern about the correct form to present statistical data. In the next two sections, we will introduce Ferrán's work on cholera and the functioning of the Prix Bréant. In section 4 we will examine Ferrán's submissions. In section 5 we will present our interpretation comparing Ferrán's data with the submission of another physician working in Spain on cholera, Philipp Hauser. The final section will present some concluding remarks.

2. The development of Ferrán's controversial vaccine

Jaime Ferrán y Clúa was born in Corbera del Ebro (Tarragona) in 1852, the son of a rural physician.⁹ He graduated in medicine at the University of Barcelona in 1873. His first medical practice was set up in the nearby Tortosa, where he also began his scientific career under the mentorship of the astronomer and geologist José Joaquín Landerer (1841-1922). Landerer gave Ferrán access to his own microscope and the *Comptes rendus hebdomadaires de l'Académie des Sciences de Paris*, where he most likely discovered the work of Pasteur. His first forays into bacteriology were vaccines for carbuncle and swine erysipelas, which Ferrán prepared in 1880. In 1884 Ferrán received an award from the Royal Academy of Medicine of Madrid for his report on bacterial parasitism. This early interest in vaccination earned Ferrán a seat in the committee that the Barcelona city council appointed to prepare for the arrival of cholera, already ravaging the neighbour regions, sending its members to Marseille in order to study the management of the epidemic.

Between September and October 1884 Ferrán worked in Marseille and Toulon under the supervision of W. Nicati (1850-1930) and M. Rietsch (1848-1905), the medical officers in charge of the outbreak.¹⁰ In their laboratory, Ferrán learnt how to prepare bacterial growth media in order to isolate the commaform bacillus that had been described

by Robert Koch shortly earlier.¹¹ This was Ferrán's induction in the methods of the international elite of cholera research: Nicati and Riesch would be competing for the Bréant with Ferrán only two years later.

The apparent immunity exhibited by the French survivors gave Ferrán the idea to develop a vaccine.¹² Disregarding the risk of spreading the disease, he brought back bacterial cultures to Tortosa. After the quarantine, probably by November 1884, Ferrán started to inoculate cholera cultures into guinea pigs in various dosages and through various pathways, observing signs of immunity. On this basis, Ferrán developed an injectable vaccine that he first tried on himself.¹³ In December 1884, Ferrán communicated his purported success to the Royal Academy of Medicine of Barcelona and the Spanish Ministry of Home Affairs (*Ministerio de Gobernación*).¹⁴ Whereas the Academy did welcome Ferrán's initiative, the Ministry remained silent. Perhaps silence simply expressed incomprehension: at the end of 1884, bacteriology was not the dominant paradigm among Spanish physicians, although Koch's ideas were already being debated.¹⁵

The Valencian cholera epidemic intensified throughout 1885.¹⁶ Advised by a local physician (Amalio Gimeno), the regional governor invited Ferrán to start a vaccination campaign. In March 1885, Ferrán set up a laboratory in Játiva and, by mid-April, he started the vaccination campaign, leading a group of Valencian physicians.¹⁷ By the end of July, the campaign estimated the number of inoculated patients to be 50.000.¹⁸ Historians like George H Bornside¹⁹ highlight the systematicity of the campaign's protocol, following Ferrán's own account.²⁰ On paper, there should have been an identification number for every patient, who, after the inoculation, would receive a certificate with basic information about the vaccine's effects.²¹ According to the initial plan there should indeed have been control over the patients's inoculation regime, which prescribed three doses in order to achieve immunity.²² Yet, as one of the team doctors observed, the demand for the vaccine was so overwhelming that it was most often administered without any record or trace.²³ In the end, the data came from the municipalities where the vaccination campaign had taken place. They provided records of diagnostics and deaths, so that Ferrán and his collaborators could estimate whether there was any difference on both accounts between inoculated and non-inoculated patients.²⁴

On 18 May 1885, only a month after the start of the campaign, the liberal opposition in Parliament took notice of the Valencian initiative and requested official support for the campaign in order to conclusively establish the efficacy of Ferrán's vaccine.²⁵ The ruling conservative party commissioned the Royal Academy of Medicine of Madrid and the Royal Health Council (*Real Consejo de Sanidad*) to investigate the vaccine's efficacy, and a report was quickly delivered –still within May. The Ministry then formed a committee to carry out the inquiry and prohibited the campaign to carry on, allowing only Ferrán to conduct individual inoculations. The report of the committee was delivered on 23 June 1885.²⁶ It acknowledged the existence of an active principle in Ferrán's vaccine, but deemed the statistical evidence provided as insufficient to demonstrate its efficacy.²⁷ Firstly, there was no official record about the number of towns affected by the outbreak, as the official notification to the provincial authorities was often delayed – if not hidden – by the town halls. Furthermore, there was no conclusive evidence about the medium- and long-term protection offered by the vaccine, since the report had to be submitted quickly. As a result, the committee called for an official statistical inquiry into the vaccine that controlled for the relevant risk factors (sex, age, residence, social class). The new report met with an even more sceptical verdict by the Royal Academy of Medicine on 21 July 1885.²⁸

In Valencia several municipalities kept requesting Ferrán's vaccine and the Government allowed him to proceed without sanction in order to avoid riots. The campaign was therefore resumed, and Ferrán continued to vaccinate from mid-April until approximately the end of the autumn.²⁹ At the request of Ferrán, a second committee was formed to accompany the campaigners on site and gather the necessary information. The second report, delivered in December 1885, reached different conclusions: there was no evidence about an adequate preparation of the vaccine, it was not harmless and yet the data gathered about its efficacy were *prima facie* positive. An external statistical advisor compared how many contagions had taken place among the inoculated and non-inoculated participants in the campaign. There had been more contagions among the latter, but the advisor thought the number of inoculations was small to reach any solid conclusion.³⁰

In November 1885, a significant event took place that would significantly affect the status of public health policies: the death of king Alfonso XII due to tuberculosis. This change in the monarchy ended a decade of political and economic stability in which the

liberal and the conservative parties took turns in government, whatever the outcome of the elections, which were often rigged. Their ideological differences were often insignificant in terms of the effect it had on health policy matters. For instance, at the time, the mortality rate in Spain was high compared to other European capitals, but neither of these two parties paid particular attention to this issue – except during epidemics. Quarantines were the policy of choice to contain outbreaks and they were often passed without prompting any substantial reform (e.g., in urban hygiene).

In this context, in May 1885, Manuel Castelar, a leader of the liberal opposition, invoked Pasteur's success in front of the Spanish parliament, and requested official support from the Government for Ferrán.³¹ France had been a major source of financial investments in Spain and, by the end of the nineteenth century, most politicians and entrepreneurs had been educated in Francophile environments. It is not surprising that Castelar was aware of the development of French bacteriology, even if he had no scientific qualification. What is surprising is how his call sparked a debate that polarized Spanish politics, with the liberals siding with Ferrán and the conservatives becoming *anti-Ferranistas*. The controversy was then amplified through several scientific bodies. The Royal Academy of Medicine of Madrid held two inconclusive sessions in July 1885. The conflict escalated to such a degree that the Spanish Society for Hygiene had to suspend its sessions to avoid clashes among its members.³²

Also in that same summer of 1885, several international delegates got in touch with Ferrán and even visited Valencia to inquire about the vaccine's success, with equally contradictory conclusions.³³ A few independent physicians published positive assessments: the French Emile Duhourcau, the Irish Charles Cameron, the British John Boyd, and the Portuguese Eduardo Abréu were positive about the vaccine.³⁴ In contrast, the representatives of the British Association for the Promotion of Research in Medicine were sceptical, since they questioned the causal responsibility of the *Kommabazillus* in the epidemics.³⁵ As for government representatives, the Portuguese delegation also remained skeptical, whereas the US delegate, Edward O. Shakespeare, was *prima facie* positive.³⁶

Among these delegations, the *Brouardel Commission* authored the most influential international report on Ferrán's vaccine.³⁷ The committee had been appointed by the French Ministry of Commerce under the presidency of Paul Brouardel (1837-1906), a preeminent professor of medicine who had already chaired the *Comité consultatif*

d'hygiène publique for the Ministry of Home Affairs in 1884, reporting on the cholera epidemics in Marseille and Toulon. Brouardel and two more physicians (J. Albarrán and P. Charrin) arrived in Valencia in June 1885. The commission probably intended to obtain some cultures and submit samples to Paris (following Pasteur’s advice). But Ferrán only allowed them to examine the cultures in his own laboratory: if the French Ministry of Commerce was interested in his method, argued Ferrán, it should directly negotiate with him a disclosure agreement. The commission focused instead on Ferrán’s laboratory as indirect evidence of his ability to produce a vaccine: they found his facilities wanting for lack of both proper equipment and guinea pigs. The commission then witnessed the inoculation of 20 nuns and visited four inoculated towns. As to the statistical data on Ferrán’s vaccination campaign, the committee found them, again, *prima facie* positive but unreliable, since, according to their inquiries, the census was probably underestimating the real population and the local authorities often lied about the number of cholera deaths in order to avoid the *cordon sanitaire*.³⁸ The Brouardel commission concluded, in July, that there was still no proof of the prophylactic value of Ferrán’s vaccine.

This conclusion triggered the nationalist account that somehow dominated the Spanish historiography of this episode. Ferrán denounced the French prejudice against Spanish innovation, praising his own “dignified attitude regarding the arrogant demands” of the French commission.³⁹ Pulido, author of the first full account of the events and a collaborator himself of Ferrán’s vaccination campaign, considered that the Commission left Paris “prejudiced” (*mal prevenida*)⁴⁰ – and still in the 1950s we find traces of this perspective.⁴¹

June 1885	Report of the Ministerio de la Gobernación committee	Not enough evidence about efficacy
July 1885	Report of the Royal Academy of Medicine	Not enough evidence about efficacy
July 1885	Report of the Brouardel Commission	No evidence about efficacy
December 1885	Report of the second committee of the Ministerio de la gobernación	<i>Prima facie</i> signs of efficacy, not conclusive

Fig.1 Summary of the official reports that triggered the controversy

Figure 1 summarizes the sceptical results of the main reports against Ferrán that were published in 1885. In the summer of 1885, Ferrán must have felt caught between

more than two fires. In his view, the political prejudices of the sponsoring Ministries (in Spain and France) spoiled the official reports on his vaccine, preventing them from acknowledging its efficacy. In this context, it seems as if Ferrán tried to settle the controversy on purely scientific grounds, invoking the authority of the French Academy of sciences with his submission to the Prix Breant. To Ferrán's eyes, the Academy must have appeared as the ultimate scientific arbiter for scientific debates. And, indeed, throughout the nineteenth century the Academy had built a system of generously endowed prizes that sanctioned scientific success internationally.⁴²

The Academy was certainly not the only international institution interested in Ferrán's vaccine. Abréu, a contemporary observer, lists fifteen other Academies in Europe and three in America that had expressed some interest in the inoculation – together with twelve medical societies, seven institutes and another seven medical schools, all outside Spain⁴³. But none of them had a prize to reward cholera research. Whereas the other Academies could simply leave the question open, the decision of the Bréant jury implied that, contrary to Ferrán's belief, his evidence did not show that he had made any fundamental discovery on cholera and, in particular, he had not found a preventive treatment. Otherwise he should have received the prize.

As we are going to see, the Academy's decision did not settle the question: Boyd, Cameron and Shakespeare published their positive assessments after the Bréant's first decisions. But let us first contextualize the Prix Bréant.

3. The Prix Bréant

The French Academy of Sciences instituted the Bréant award in 1854 with a 100.000 francs donation from a successful chemist, Jean-Robert Bréant.⁴⁴ The applicant could win the total amount in three cases: if they submitted a cure for cholera (effective in most cases); if they discovered its causes in such a way that if these latter were suppressed, the epidemics would cease; or if they found an effective prophylaxis. Outside these three cases, the Academy could reward any progress on the causes of epidemics with the annual interests of the endowment (about 5000 francs). There were also *mentions*, *récompenses* and *encouragements* of a lesser amount. In the 1880s, the Bréant was the Academy's best-funded award, but nobody ever won it in full.⁴⁵

The jury was appointed every year among the members of the *Médecine et Chirurgie* section of the Academy, usually five or six physicians.⁴⁶ Between 1884 and 1888, our period of interest, three of the members were present every year (E.-J. Marey,

D. Richet & J.-M. Charcot). Ch.-E. Brown-Sequard took part in three deliberations and A.-L. Gosselin and E. Vulpian in two.⁴⁷ The jury members in this period were all middle-aged (above 50) and many of them close to retirement –the Academy was a traditionally gerontocratic institution.⁴⁸ They shared institutional affiliations (*Faculté de Médecine de Paris, Académie Nationale de Médecine*) and academic endeavours like the *Association Française pour l'Avancement des Sciences*, which counted three jury members among its chairs –A. Verneuil, Ch.-J. Bouchard and J. Marey.⁴⁹ Some of them had certainly achieved scientific pre-eminence: according to Grmek and Fantini, Vulpian, Brown Séquard and Charcot were among the leading clinical experimentalists in France. The scientific outlook of the jury was therefore stable during those five years.⁵⁰

The deadline for submissions to the Bréant, like other awards of the Academy, was set on 1 June, although it was not strictly enforced.⁵¹ The submissions were compiled in a folder, which was then filed in the archives together with the minutes of the jury. In the minutes, the author and title of the submissions were listed and numbered together with the jury's assigned referee. The minutes were closed with the award decision signed by all the jury members. As for the assessment of each submission, there is no discernible pattern: sometimes it was a simple score, sometimes a full report and sometimes there was simply nothing. The awarded submissions were published in the Academy's *Comptes Rendus Hebdomadaires*, with a list of the jury members, the submissions's referee and a short justification of the award, followed by the customary formula "The Academy adopts the conclusions of this report" (*L'Académie adopte les conclusions de ce Rapport*).

The awards of the two years previous to Ferrán's first submission exhibit an interesting range of responses from the jury. In 1883, the Bréant was awarded to a submission on the aetiology of cholera authored by S.-A. Fauvel, the French general inspector for health services. At the same time, the Academy recognized the efforts of some of the members of the failed French scientific expedition to Egypt for the study of the 1883 cholera epidemics (the so-called *Mission Pasteur*, although Pasteur himself remained in France). Given the lack of clear scientific outcomes, this seems like an award to the courage of the expedition, where one of its members died.⁵² In contrast, in 1884 the Bréant was not awarded for a lack of deserving submissions, even if the dossier reveals that a high officer of the French Ministry of Finance (a certain Seray) was supporting one of the applicants (S. Perrone) with a letter of recommendation.⁵³ In other words, the jury was both capable of both endorsing and resisting non-scientific considerations.

As for the number of applicants in the period considered, it peaked around 1885 (41) and 1886 (44), the years of the cholera epidemics in France and Spain. In prior and later years, it never went beyond 10 candidates. Ferrán first tried his chances unsuccessfully in 1885, only to obtain the distinction in 1907. To contextualize our discussion of Ferrán's early misfortunes with the Bréant, it also helps to consider the identity of the winners.⁵⁴ In 1885, the mention was awarded to J. Mahé, a former student of the leading French neurologist J.-M. Charcot and French delegate in a number of international conferences on epidemics, for his *Mémoire sur la marche et l'extension du choléra asiatique des Indes orientales vers l'occident*, a report commissioned by the French Ministry of commerce. Still in 1885, there were three encouragements (endowed with 1500 francs) to three memoirs on such diverse topics as the ingestion of a diarrheic cholera solution, a statistical study on cholera admissions in Parisian civil hospitals, and the presence of bile salts in the blood of cholera patients. All three authors had a French name (Bochefontaine, Rivière and Pouchet). In 1886 there were three *récompenses* for memoirs on the cholera epidemic of 1884. In 1887, two bacteriological memoirs received encouragements, one by Victor Galtier (a competitor of Pasteur⁵⁵) and a joint work by two French physicians: A. Chantemesse, a disciple of Pasteur, and A. Widal.⁵⁶ In 1888, the Academy distinguished Philipp Hauser.

All in all, between 1884 and 1910, 54 candidates received part of the award (only seven of them got a 5000 francs prize). Almost all of them were male, and most of them were physicians. Interestingly, only 16 of their memoirs were directly on cholera and, as we just have seen, both the topics and the approaches vary. There were, for instance, studies on tuberculosis (4), typhus (4), tetanus (3), rabies (3), plague (2), smallpox (2), and cancer (1). On cholera we find not just inquiries on vaccines, but also histories of epidemics, statistical studies, analyses of health organizations and even awards to a career, as it was the case of Ferrán's 1907 distinction. There is not much geographical diversity: at least, eighteen of the awardees (33%) were working in mainland France. In the minutes of the years we have examined there is often a significant proportion of foreign applications: for instance, 30% in 1884 and 51% in 1885.

4. Ferrán's submissions to the Prix Bréant in the 1880s

Ferrán made three submissions to the award, all but one of them in French (in 1885, 1886 and 1907) and a letter to the jury in 1888. The first two were dismissed and the third one received a mention.

1885	Four separate pieces dated on 31 March (1), 10 July (2), 28 July (3) 23 August (4) Discussion at the Academy: 13 April (1), 13 July (2) 31 July (3) Final report: undated (around October 1885)
1886	One piece dated on 13 January Discussion at the Academy: 18 January Final report: undated
1907	One piece, submitted on 3 June Discussion at the Academy: No file available Final report: 2 December

Fig.2 Chronology of Ferrán's submissions

As we are going to see, the fate of Ferrán's early submissions was probably sealed with his first try, where he presented his vaccine as the culmination of his early research on cholera. The examination of the archival record attests to the interest of the jury in his vaccine: the submission arrived in batches, half of them beyond the deadline. Nonetheless, the assigned reviewer took time to consider them all and expand on the initial assessment. The report of Ferrán's submitted memoirs in 1885 turned out to be unusually long and thorough, in stark contrast with the two subsequent assessments –a brief comment in 1886, and no comment at all in 1888.

Ferrán was listed 23rd among the forty one applicants for the 1885 Bréant.⁵⁷ His submission fills the bulkiest folder in the archive (the 23rd). There are three different essays: one on the pathogenesis and prophylaxis of the *Kommabazillus*; another on the subcutaneous injection of live cultures for prophylaxis; and a final piece (in two parts) on a chemical vaccine against cholera. His assigned referee was A. L. Gosselin (1815-1887), a Parisian professor of pathology and a decade-long member of the Academy, of which he would become president of the medicine section in 1887. He was also faculty at the *École Supérieure de Pharmacie de Paris* and an *Hôpitaux de Paris* surgeon since 1851. Since 1860, he had been also a member of the *Académie Nationale de Médecine*.⁵⁸ Gosselin was a clear representative of the Parisian medical establishment. Although we cannot be certain as to his grasp of Pasteur's approach, his unusually long review of Ferrán's submission exhibits indicates a skilful control of both general methodological principles, expert testimony, and indirect evidence. His preliminary reports were discussed on the sessions of 13 April, 13 July and 31 July, and he must have finished

writing his review by the end of the year (the document is not dated, but it contains observations from as late as 9th October).

In his first piece, dated on March 1885, Ferrán studied the effects of subcutaneous injections of two types of cholera cultures on guinea pigs, trying different dosages.⁵⁹ He performed a comparative experiment in which he infected an inoculated group of rabbits and a control group with cholera, with the former surviving the disease, unlike the latter. Gosselin found the experiment *prima facie* persuasive but wanted details about both the cultures preparation and the evaluation protocol. Ferrán also reported the inoculation with this culture of forty-two healthy human subjects (among them, Ferrán himself and his wife) without noticeable adverse effects. The regime consisted in two 0,5cc injections on each arm within eight days. Gosselin was more sceptical about this vaccine, citing the experiment of two distinguished physicians who had tried to inoculate guinea pigs with samples of Ferrán's vaccine they had brought from Valencia. Their animals died with symptoms of cholera.⁶⁰

Ferrán submitted an additional piece in July reporting the development of another vaccine with a different culture and dosage.⁶¹ This time, the administration regime consisted of three injections on both arms of the patient within five days. Gosselin again missed details about the culture and data on the effects, which Ferrán promised to submit, but never actually did. After receiving the new document, Gosselin irritatingly wondered why Ferrán was withholding the publication of his data.⁶²

By the end of that same month of July, Ferrán sent the third piece reporting the development of a chemical vaccine developed with dead cholera microbes.⁶³ Interestingly, there is an annotation on the document reading 'Concours Bréant 1886', arriving as it had so well past the official deadline (1 June). Yet, Gosselin incorporated this piece into the 1885 dossier, although with growing impatience. What is the point of yet another vaccine, wondered Gosselin: "We, the jury of the Prix Bréant, only need one thing, the proof by authentic facts of the first positive statements of April 13 and July 13 [the first two submissions on the original vaccine]."⁶⁴

At this stage, Gosselin had started to gather whatever indirect evidence he could find on its effects. First, he considered press clips: in the dossier we find a cutting from the French newspaper *Gaulois* (17 July 1885) with a very positive appreciation of Ferrán's vaccination campaign in Benifayó (Valencia) based on Ferrán's own data. Gosselin was well aware about how unusual this source was: "Unquestionably, it is not

our custom, and should not be, to use these sources. But given that Mr. Ferrán, knowing about our scientific customs, has reached out for these publicity outlets, and since the issue is too important to neglect any piece of information, we have sought on that side and this is what we have found.” Yet, asked Gosselin suspiciously, why would Ferrán provide statistical data to a journalist, withholding them from the Academy?⁶⁵

In addition to press clips, Gosselin referred to medical sources from Spain. In the dossier we find a copy of a speech by the physician Antonio Sierra y Carbó to the Spanish Society of Hygiene, delivered on 1 August 1885, in which the author comments sceptically on Ferrán’s synthesis method for the vaccine.⁶⁶ Gosselin also referred to the equally sceptical report of the Royal Academy of Science of Madrid previously discussed in section 2.

Finally, Gosselin included the already mentioned note presented by Gibier and van Ermengem at the Academy of Science on 18 August in the dossier, and another note read by Chantemesse at the *Académie de Médecine* on the chemical analysis of Ferrán’s vaccine.⁶⁷ Gosselin referenced Brouardel’s intervention at the *Académie de Médecine* on 7 July, summarising his negative report about his visit to Valencia. Despite the interest Gosselin took in Ferrán’s submission, all the indirect evidence Gosselin could gather spoke against Ferrán’s method, as it transpires in the report’s closing paragraph: “[Ferrán] has provided neither true nor personal outcomes, and when we have requested them, he has answered with theoretical studies and hypotheses for which we hadn’t asked. Under these circumstances, the Commission decides unanimously not to award the Tortosa physician the 100.000 francs endowed by M. Bréant for the person who found the way to cure or eliminate cholera.”⁶⁸

Gosselin’s review contains an annex of a few extra pages, numbered with letters instead of figures, with some additional consideration that, nonetheless, didn’t change the initial conclusion. The reason for the annex was the arrival of the long-demanded statistics of the vaccination campaign in Valencia on the 23rd August. The data roughly covered the interval between 1st July and 5th August (five weeks) in seven different towns. Ferrán submitted the data in quite a peculiar format: for each town in which he vaccinated, there was a document with several figures authenticated by the town’s registrar (sometimes also signed by the town’s major, physician and priest). The recorded data varied from town to town, but the document generally included the number of inoculations, the number of cholera contagions and deaths among inoculated and non-inoculated people,

plus the town's census.⁶⁹ The campaigners chose to re-inoculate after five days, instead of eight as in the first submission. Yet, in several towns, the campaigners only inoculated once. There was no other information about the vaccinated patients and no follow-up after five weeks.

Moreover, the data were not tabulated for analysis.⁷⁰ Gosselin included his own calculations for the proportions between inoculated and non-inoculated subjects among contagions in the dossier. In places like Cheste or Chiva it seemed partially positive for the vaccine: it apparently prevented contagion, but if there was an infection, people died in similar proportions with and without the vaccine. Yet, in Chiva, the vaccine had only been administered once, against the initial administration regime.⁷¹ In towns with the two prescribed inoculations, the results were instead contradictory. Gosselin added up the data from the seven towns: there had been 42,294 vaccinations, of which only 1,4% had contracted cholera, in contrast to 9% of the non-vaccinated census who contracted the disease. Gosselin remained sceptical: the data did not seem conclusive. On 1st October, when he was finally closing his report, Gosselin observed that the epidemic was still ongoing in Spain and there was no information about the protective effects of the vaccine. Would not have Ferrán or the press alerted about it if there had been any, he wondered?⁷² The 1885 review was definitely closed with a negative.

With all these antecedents, it is not strange that Ferrán's submission the following year, in 1886, "Le principe actif au Komabacille [*sic*] comme cause de mort et de l'immunité" (jointly authored with the chemist Inocente Paulí) was dispatched by the reviewer (Gosselin, again) with just a few dismissive lines and a 00 score.⁷³

Yet, although this was not a formal submission, Ferrán would send a letter to the 1888 jury, prompted by a priority dispute.⁷⁴ Pasteur triggered it with his intervention at the Academy, commenting on "Sur la vaccination préventive du choléra asiatique" by the Russian bacteriologist M. N. Gamaleïa (1859-1949).⁷⁵ Pasteur recommended Gamaleïa for the Bréant and offered his laboratory so he could reproduce his experiments in inoculated pigeons. Once published in the *Comptes Rendus*, Ferrán reacted with a letter to the jury on 9th October 1888,⁷⁶ reminding them of his previous submissions and inviting them to respect his priority rights on the cholera vaccine.⁷⁷ Further letters of support were received.⁷⁸ The Barcelona Medical Conference (15th September 1888) asked the Academy to invite Ferrán to reproduce his experiments in equality of opportunity with Gamaleïa. The Royal Academy of Medicine of Barcelona submitted a comparison

between Ferrán and Gamaleïa's experiments, regretting that Pasteur had neglected the former. Although Pasteur appears in the *Comptes Rendus* as a jury member for the 1888 Bréant, his signature does not appear in the final *bordereau du Prix Bréant* 1888, where he also does not feature as reviewer.⁷⁹ Perhaps he abstained in order to avoid a conflict of interest, although there is no mention of the reason in the private notes of the *Comité Secret*. In any case, although Ferrán had sent a letter more than a formal submission, he did not receive any attention from the jury (and Gamaleïa received no award, either).⁸⁰

In 1907, almost twenty years after his last attempt, Ferrán submitted to the Bréant a note on the longevity of cholera bacteria. The text is not in the Academy's archive, although it is mentioned in the minutes and the *Comptes rendus*.⁸¹ His assigned reviewer was Emile Roux, a Pasteurian bacteriologist. Among the jury members, only Bouchard had been part of the 1880s jury. Roux remained appreciative of Ferrán's work⁸² and exchanged respectful letters with him.⁸³ The *Comptes Rendus* make an explicit mention of the 'list of works on cholera [that Ferrán] published since 1884', acknowledging Ferrán's priority in showing the pathogenic action of Koch's vibrio on animals and the possibility of immunization both on animals and humans.⁸⁴ The jury remained nonetheless silent on the efficacy of his vaccine. The historian Lopez Piñero considers this retrospective award the consequence of the appeasement of earlier scientific nationalism.⁸⁵

5. Chauvinism or biased data?

The standard historical interpretation of Ferrán's early failure at the Bréant originates in Ferrán's own account, where he claimed that the Academy would have just chauvinistically sided with the Brouardel commission, because a Spaniard could not seize the priority of the Parisian school of bacteriology in anti-cholera vaccination.⁸⁶ This is also the interpretation that we find in the earliest history of the episode, written by a collaborator of Ferrán in the Valencian campaign.⁸⁷ In more recent and sophisticated analyses, chauvinism is diluted into nationalism in the broader context of political competition in late nineteenth century European science.⁸⁸ Still, historians like Fernández Sanz⁸⁹ continue to side with the aggrieved version of Ferrán and Pulido, while López Piñero blames Ferrán's lack of recognition on a combination of nationalism and a patronizing attitude regarding the underdeveloped status of Spain.⁹⁰ Of course, there are more ingredients to this narrative: e.g., to name just one, the lack of official support (and resources) prevented Ferrán from organizing his vaccination campaign in a more

systematic manner that would have delivered the necessary statistics.⁹¹ And not every Spanish historian endorses the chauvinistic narrative about Ferrán's unacknowledged merits.⁹²

This interpretation is, of course, defensible if interpreted in terms of strict scientific encouragement: if the goal was to incentivize cholera research, the Academy should have awarded Ferrán the prize, and it seems plausible to conjecture that if he had been French, he would have obtained at least a Bréant *mention* or *encouragement*. Yet, the accusation of chauvinism against the Academy runs somewhat deeper, claiming that the jury's nationalism led them to actively neglect the evidence that Ferrán presented, which demonstrated the vaccine's positive effects. The strongest case for this account is Bornside's, which provides a statistical reanalysis of the data from Alcira's vaccination with positive results.⁹³ Although Bornside includes some methodological caveats about the lack of controls in Ferrán's campaign in his argument, he considers the Spanish physician's vaccine a success, to a degree comparable to those of modern vaccines.⁹⁴

We think it is time to revise Bornside's account and the accusations of chauvinism against the Bréant jury. In our view, even if the Academy was an instrument of French scientific diplomacy, there is no evidence that Gosselin was blinded by nationalism in his assessment of Ferrán's vaccine. We would rather say that Ferrán and his supporters – both historical and contemporary – were falling prey to some well-known statistical biases that were already appreciated by his contemporaries. Furthermore, as we have shown, there is evidence that the Academy was sensitive to the presence of biases in statistical data, independently of the nationality of the applicant.

In the first instance, we should bear in mind that the jury could not directly examine Ferrán's method for synthesizing the vaccine, which was a *secret remedy* for all practical purposes. The assessment of its efficacy depended entirely on the available data, of which the *Ferranistas* have been traditionally uncritical, often falling prey to a form of what we would call today *selection bias*. Both Ferrán at the end of the nineteenth century and Bornside almost a century later used those records that seemed *prima facie* most positive for the efficacy of the vaccine, taking them at face value. But, as we would put it today, this sample is not representative of the full range of effects of the vaccine. This is no anachronism, since the mistake had been already appreciated by Ferrán's contemporaries. The report of the first official Spanish committee in 1884 pointed out that the unvaccinated rich were less vulnerable to cholera, and yet they had been

vaccinated more often than the poor in Valencia, thus biasing the comparison between the two. Pasteur himself had warned Ferrán about not comparing patients *like with like*, in a letter dated on May 23th 1885.⁹⁵ As Gosselin observed, in the data there also seemed to be evidence about lack of efficacy that Ferrán simply discounted – as did Bornside in his historical interpretation. Moreover, Gosselin suspected that Ferrán was selectively reporting the data, instead of disclosing the full statistical record.⁹⁶ Ferrán's Valencian campaign had started in April 1885, with the number of inoculated patients reaching the thousands within four months. At the end of the campaign, Ferrán had collected data on, at least, 28 towns. He only submitted the records of seven municipalities to the Bréant, although, as Gosselin observed, he was releasing partial data to journalists and to the different committees inspecting his campaign.

In our view, given the available data, we will remain forever agnostic about the efficacy of Ferrán's vaccine: it is impossible to determine whether it worked or not. Among the many sources of uncertainty, we should bear in mind those already noticed by Ferrán's contemporaries: the local census was unreliable; there were lots of out-of-protocol vaccination (most of the towns reported just one injection, instead of two or three); there was no reliable diagnosis of cholera and no accurate data on its prevalence; and there was not enough information about potential confounders. For all these reasons, the Valencian data did not allow Gosselin – and do not allow us today – to find out whether Ferrán's vaccine worked. Consequently, we argue that the history of Ferrán's vaccine should remain agnostic about its efficacy – an agnosticism that is precisely what we find in the Academy's assessment.

The question then remains: was this agnosticism a methodological excuse to disguise the jury's chauvinism? We believe the answer is no. If this had been the case, the Academy could have been equally agnostic about Philipp Hauser's (1832-1925) submission studying the 1885 Spanish cholera outbreak. Instead, he obtained a Bréant *récompense* in 1888. Although born in Nàbasdan then at the Austro-Hungarian Empire (now Trstín, Slovakia) and educated in Vienna, Paris and Bern, Hauser had been working in Gibraltar, Seville, and Madrid since 1861 and already had the Spanish nationality. It is open to discussion whether the cosmopolitan Hauser could have triggered any chauvinistic reaction in the jury. What is certain is that he received the award for a Spanish publication, his three volume study *Estudios Epidemiológicos relativos a la etiología y*

profilaxis del cólera.⁹⁷ Let us briefly discuss his application and the reasons for his success.

Hauser was a disciple of Max von Pettenkofer (1818-1901), a pioneer in public health who established the field of experimental hygiene, for whom time cycles and the composition of soils was the primary factor to explain the spread of choleric miasmas. For Pettenkofer's school, the main source of evidence was the tabulation of cholera figures according to the types of soil, which allowed them to document how cholera spread faster in the most propitious regions.⁹⁸ This was also Hauser's strategy: he mobilized his extensive social network in Madrid to gather the necessary data for his study. One of his patients, Arcadio Roda, was Director for Beneficence and Health at the Ministry of Home Affairs in 1885. Hauser persuaded him to send a questionnaire to all the physicians and mayors of the municipalities affected by the outbreak. Hauser drafted twenty four of the questions and the Ministry added a few more, and sent out 2000 letters. Hauser also involved some regional governors of whom he was a personal friend,⁹⁹ and even reached an agreement with the United States delegate charged with the study of the Spanish epidemics, persuading him to share the printing expenses of his volumes in exchange for the primary data.¹⁰⁰

All this data made its way into three bulky volumes. In the first one, Hauser described the development of the epidemic in the different Spanish provinces, comparing the intensity and duration in each town with its health conditions and fluvial and geological characteristics. The second volume contained statistical data from the different provinces: monthly figures of the cholera fatalities and infectious diseases recorded between 1880 and 1884. The data were then (informally) analysed for any correlation with the health and soil conditions. The third volume presented the primary sources for the study (the responses to the questionnaires) and a set of eighteen maps documenting the spread of the epidemic. Hauser's *Estudios* were not merely descriptive. He intended to find "the laws ruling the development and spread of the cholera epidemic".¹⁰¹ The evidence he found persuaded him of the truth of Pettenkofer's approach, inviting him to preface the second volume of the *Estudios*.

Unfortunately, the submission file with all the reports is not preserved in the archive. The only remaining record is a cover letter from Hauser to the jury, in which he points out that he makes a submission to the Bréant at the request of one jury member, Charcot, who would later assess his submission.¹⁰² According to the decision published

at the *Comptes rendus*, Hauser's *Estudios* deserved the encouragement for its impeccable method in both the gathering and the analysis of the data.¹⁰³ Even if, in the jury's opinion, the problems that Hauser intended to tackle were not "fully solved" and his conclusions were often "at odds with the generally established views", his *Estudios* so thoroughly established the facts about the Spanish outbreak that it became a reference work for "any physician interested in the etiology and spread of cholera".

Interestingly Hauser was awarded a 3000 francs *récompense*, but not the full 5000 francs of the endowment's interest for the year. There is no similar decision in the Bréant award records.¹⁰⁴ This is, perhaps, indicative of the mixed feelings of the Jury, who were impressed with the statistical achievement but not so much with the theoretical outlook. Two members of the jury held opposite views to Hauser: Marey believed in the role of waterflows in spreading the diseases;¹⁰⁵ and Bouchard didn't accept the causal role of Koch's bacillus – which Hauser did, but in combination with soils.¹⁰⁶ As a matter of fact, in private correspondence with Pettenkofer, Hauser expressed his surprise at the decision.¹⁰⁷ Nonetheless, the award contributed to his international reputation, consolidated years later with the Pettenkofer prize awarded by the city of Munich in 1898 to his *Études épidémiologiques*.¹⁰⁸

Hauser's data are as thorough as it was then possible, and still serve as the official statistical record of the epidemic in Spain. Whereas statistics was not formally taught at the University of Barcelona when Ferrán received his degree,¹⁰⁹ data tabulation was crucial for Pettenkofer's school, and Hauser made the most of this approach in a context where simply gathering the data was already a significant challenge. In our view, Hauser's award signals that the Bréant jury was, at least this time, sensitive to data biases, even if the candidate had a complicated national background¹¹⁰: born in Austria, but with Spanish nationality and evaluating a German theory with Spanish data.¹¹¹

6. Concluding remarks

According to Hess, by the 1880s physicians in France and Germany were starting to count data from files and archives as clinical observations.¹¹² The controversy surrounding Ferran's vaccine provides an interesting illustration over what counted as good clinical observations for the assessment of a treatment's efficacy. For the Ferranistas – as well as many concurring historians – a collection of heterogeneous registrar's records served as more than enough evidence for the success of Ferrán's vaccine. In contrast, the Academy defended an agnostic view over such a dataset and encouraged more systematic

data collections instead, like Hauser's, independently of the theoretical approach defended.

As innovative as his approach to cholera vaccination was, Ferrán had chosen to be judged not by his (never fully disclosed) method, but rather by the efficacy of the vaccine, as shown in the Valencia campaign records. Ferrán submitted his data in a way that suggested selective reporting. We cannot rule out, of course, that the jury members shared more or less implicit prejudices against Ferrán, but we have found not explicit expression in the Academy's archive. We would rather say that the Bréant reviewer exhibited both patience and thoroughness in handling Ferrán's first submission.

Hence, accusing the Academy of national prejudice against Ferrán seems, in our view, ungrounded. The Bréant may have been a tool of French scientific diplomacy: it probably gave preferential treatment to French (or, perhaps, just Parisian) candidates, perhaps at the expenses of foreign applicants with more merit. Our case study just shows that the Academy was not inexorably led by nationalist considerations. Gosselin's methodological considerations about Ferrán's data are still defensible, well beyond Gosselin's own national prejudices. Perhaps it is possible to explain Hauser's award in terms of his alignment with French academic interests, but there is no direct evidence of such alignment. However, the quality of his statistical study is still unanimously praised. Nationalism may have been a strong driver in the Bréant jury's decisions but, as our two cases illustrate, it was not powerful enough to preclude the occasional appreciation of methodological quality.

NOTES

¹ 1. We draw on three main archives: The Dossiers Prix Bréant (Service des Archives, Académie des Sciences – Institut de France, Paris); the Fons Jaume Ferran (Museu d’Història de la Medicina de Catalunya, Terrassa); and the Pettenkoferiana collection (Handschriftensaal, Bayerische Staatsbibliothek München). We refer to the Dossiers Prix Bréant using the year and the candidate number assigned by the jury -handwritten in every page from the same submission. The Ferrán archive (*Fons Jaume Ferran*) is not yet fully catalogued, but we provide the reference numbers when available. All translations into English are our own, unless otherwise stated.

² 2. E. Rodríguez Ocaña, “Ferrán y Clúa, Jaime” in *Dictionary of medical biography*, vol. 2, ed. W. F. Bynum & H. Bynum (Westport, Conn.: Greenwood Press, 2007), 486-488. Ferrán signed his scientific works with the Spanish “Jaime”, instead of the Catalan “Jaume”.

³ 3. M. Echenberg. “Cholera: Fourth through sixth pandemics, 1862-1947” in *Encyclopedia of pestilence, pandemics, and plagues*, ed. J. P. Byrne (Westport, Conn.: Greenwood Press, 2008), 111; C. Hamlin *Cholera: the biography*. (Oxford ; New York: Oxford University Press, 2009), 236-242

⁴ 4. J.J. Fernández Sanz, *1885, el año de la vacunación Ferrán: trasfondo político, médico, sociodemográfico y económico de una epidemia* (Madrid: Fundación Ramón Areces, 1990); J.M. Lopez Piñero, “Presentación. La vacunación anticolérica de Ferrán en la historia de la salud pública” in J. Ferrán y Clúa, *La inoculación preventiva contra el cólera morbo asiático* (Valencia: Conselleria de Sanitat i Consum, 1985), 3-10; Á. Pulido *¡Vae inventoribus magnis! La odisea de un descubrimiento médico grandioso: el doctor Ferran y el cólera morbo asiático en la Guerra europea* (Barcelona: Imprenta La Reinaxença, 1921).

⁵ 5. From now on, we will refer to the French *Académie des Sciences* in English (or, shortening, *the Academy*).

⁶ 6. For an overview of the emergence of statistical epidemiology, see. A. Morabia, ed. *History of Epidemiologic Methods and Concepts* (Basel: Springer, 2004). As to the Parisian scene, there is an updated overview in M. Corteel, *Le hazard et le pathologique* (Paris: Sciences Po, 2020). For the history of public health statistics in nineteenth century Spain see E. Rodríguez-Ocaña and J. Bernabeu Mestre, "El 'legítimo criterio aritmético'. Los métodos cuantitativos en la salud pública española, 1800-1936" *Quinto Encuentro Marcelino Pascua. La Epidemiología y la Estadística*, ed. E. Sánchez-Cantalejo, (Granada: Escuela Andaluza de Salud Pública, 1996), 9-33. Ferrán's own statistical training in Barcelona must have been minimal: see T. Corbella Domenech, "Antecedentes de la enseñanza de estadística en las universidades de Cataluña", *Historia de la probabilidad y la estadística (III)*, ed. J. Santos del Cerro and M. García Secades (Madrid: Delta, 2006), 259-269.

⁷ 7.V. Hess and J. A. Mendelsohn, "Case and series: Medical knowledge and paper technology, 1600–1900," *History of science*, 48, 2010: 287-314. See also V. Hess, "A Paper Machine of Clinical Research in the Early Twentieth Century," *Isis*, 109(3), 2018: 473-493.

⁸ 8. U. Tröhler, *To Improve the Evidence of Medicine: The 18th Century British Origins of a Critical Approach* (Edinburgh: Royal College of Physicians of Edinburgh, 2000); "Quantifying Experience and Beating Biases: A New Culture in Eighteenth-Century British Clinical Medicine". In *Body Counts: Medical Quantification in historical and sociological perspective*, eds. G. Jorland, A. Opinel, and G. Weisz (Montreal: McGill University Press, 2005). For our own view, see D. Teira, "Debiasing methods and the acceptability of experimental outcomes," *Perspectives on Science*, 24(6), 2016: 722-743.

⁹ 9. The main source on Ferrán's cholera research is the 1985 reprint of his 1886 monograph: J. Fernán y Clúa, *La inoculación preventiva contra el cólera morbo asiático*, (Valencia: Conselleria de Sanitat i Consum, 1985), eds I. Paulí, I Galceran, J. M. López Piñero, & A. Gimeno, prefaced with commentaries by contemporary scholars. An account of Ferrán's contribution together with a set of classified sources from the Ferrán Archive is J. Sánchez Aldeguer, *Nuevas aportaciones sobre los trabajos de Jaime Ferrán en los inicios de la inmunoterapia humana (1883-1887)*, (Bellaterra: Publicacions de la Universitat Autònoma de Barcelona, 1991).

¹⁰ 10. George H Bornside, "Jaime Ferran and preventive inoculation against cholera," *Bulletin of the History of Medicine*, 55(4), 1981: 516-532; Sánchez Aldeguer, *Nuevas aportaciones*, 74-82.

¹¹ 11. Sánchez Aldeguer, *Nuevas aportaciones*, 79.

¹² 12. There is a chapter on immunity in Ferrán y Clúa, *La inoculación preventiva*, 29-40, where he lists what he considers the four main accounts: the exhaustion of the medium in which the infectious agents live (Duclaux); the antidote left in the organism by a first infection (Klebs); a cellular modification that prevents new infections (Grawitz); the proliferation of phagocytes caused by a first infection (Bordoni, on the basis of the facts observed by Metschnikoff). According to his own testimony, Ferrán initially sided with Duclaux, but then developed his own view, in which the immunity would be a general resistance to infection due to any of the causes considered in the three remaining accounts. As far as we can tell, Ferrán's approach left no trace in the international debate on immunity that peaked in the following decade.

¹³ 13. Ferrán never published in full his method for synthesizing the vaccine (Ferrán y Clúa, *La inoculación preventiva*, 139-141), apparently in order to prevent its commercialization. This was an endless source of controversy, as we will later see. Although in 1885 Ferrán had engaged in a controversy with Koch on the *Kommabazillus* cycle (attracting Koch's attention, according to Sánchez Aldeguer, *Nuevas aportaciones*, 94-124), his initial vaccine preparation procedure seems to have been inspired mostly by French authors, using heat to attenuate bacteria -in *La inoculación preventiva*, he cites Pasteur, Chauveau and Thuillier. His views in this regard seem to have quickly evolved: in the third dossier submitted to the Academy in 1885 -see note 22-, he claims to have used dead, instead of attenuated microbes. He did not justify this change. In any case, his attenuation procedure (even if never fully disclosed) has been occasionally cited as an antecedent both by his contemporaries (e.g., as Behring's precursor, in G. Klemperer, *Berliner Klinische Wochenschrift*, 50 (1892): 1266) and in more recent accounts -e.g., J. Théodorides, *Des miasmes aux virus. Histoire des maladies infectieuses* (Paris: L. Pariente, 1991), 118.

¹⁴ 14. Ferrán y Clúa, *La inoculación preventiva*, 177-191

¹⁵ 15. E. Rodríguez Ocaña, "The social production of novelty: diphtheria serotherapy, 'herald of the new medicine'," *Dynamis*, 27 (2007): 021-031.

¹⁶ 16. It reached its peak in the summer of 1885 and finished in December. The epidemics killed about 120.000 people (0,72% of the 1877 census) (Fernández Sanz, 1885, 266).

¹⁷ 17. Pulido, *Vae inventoribus*, 77-80. Among them, S. Ramón y Cajal.

¹⁸ 18. López Piñero, "Presentación", 182.

¹⁹ 19. Bornside, "Jaime Ferrán", 522.

²⁰ 20. Ferrán y Clúa, *La inoculación preventiva*, 145-148.

²¹ 21. In the Ferrán Archive there is indeed a copy of a vaccination stub, but no other material from the campaign –see Sánchez Aldegue, *Nuevas aportaciones*, 28.

²² 22. Ferrán changed his mind as to the number of doses. In the initial March submission, they were two (Ferrán y Clúa, "Sur l'action pathogène et prophylactique du bacille-virgule. Lettre de M. J. Ferrán. Séance du lundi 13 avril 1885. Memoires présentés," *C R Hebd Seances Acad Sci C*, 1885, 959; "Sur l'action pathogène et prophylactique du bacillus-virgule", together with a letter in French, dated in Tortosa, on 31 March 1885, Dossiers Prix Bréant, 1885, candidate 23). In July he raised it to three (Ferrán y Clúa, Note sur la prophylaxie du choléra au moyen d'injections hypodermiques de cultures pures du bacille virgule, dated in Madrid, 10 July 1885, Dossiers Prix Bréant, 1885, candidate 23; "Sur la prophylaxie du choléra au moyen d'injections hypodermiques de cultures pures du bacille-virgule. Note de M. J. Ferrán. Séance du lundi 13 juillet 1885. Memoires présentés," *C R Hebd Seances Acad Sci CI*: 1885, 147).

²³ 23. Pulido, *Vae inventoribus*, 112-115.

²⁴ 24. Fernández Sanz, 1885, 145-147.

²⁵ 25. Pulido, *Vae inventoribus*, 317-319.

²⁶ 26. F. Alonso, F. Castellote, A. Maestre de San Juan, E. García de Sola, & A. San Martín, "Memoria que presenta al Excmo. Sr. Ministro de la Gobernación la Comisión oficial nombrada para estudiar la profilaxis del cólera morbo asiático, según el procedimiento del Doctor Ferrán," *Gaceta de Madrid*, 211(July 30), 1885, 300-307. See also Ferrán y Clúa, *La inoculación preventiva*, 194-199.

²⁷ 27. At the committee there was an expert (Antonio Mendoza) familiar enough with the bacteriology of Koch and Pasteur who questioned the foundations of Ferrán's

technique. As we will see, his objections were later taken up by the Bréant examiners in 1885.

²⁸ 28. Real Academia de Medicina, Untitled report on J. Ferrán's vaccine + Minority report + Comments by the President, *Gaceta de Madrid*, 211(July 30): 1885, 307-310.

²⁹ 29. The dates are not clear: the campaign was aborted on 28 June 1885, but the second committee accompanied the campaigners during the summer (Ferrán y Clúa, *La inoculación preventiva*, 281-330). In August, Ferrán was allowed to vaccinate in Segorbe in order to avoid riots (Ibid., 303). The last record in the campaign log is from Linares, dated on 13 October (Ibid.).

³⁰30. Ibid., 230-231. For other scientific assessments of the vaccine see J.M. López Piñero, *Santiago Ramón y Cajal*, (Valencia-Granada: Universitat de València-Universidad de Granada: 2006), 184-191.

³¹ 31. Pulido, *Vae inventoribus*, 287; Rodríguez Ocaña, "Diphtheria serotherapy", 26). For a general discussion of Spanish health politics at that time of the controversy, see Hedwig Herold-Schmidt, *Gesundheit und Parlamentarismus in Spanien. Die Politik der Cortes und die öffentliche Gesundheitsfürsorge in der Restaurationszeit (1876-1923)* (Husum: Matthiesen Verlag, 1999).

³² 32. For a full discussion of the controversy around Ferrán's vaccine see Fernández Sanz, 1885. Yet, knowing what we do about the multiple factors driving political polarization, it is hard to tell whether the crisis of the conservative party is enough to explain why it rallied against Ferrán.

³³ 33. See Bornside, "Jaime Ferrán", 525-529; Fernández Sanz, 1885,. 135-145; Ferrán y Clúa, *La inoculación preventiva*, 177-269; C. Hamlin, *Cholera: the biography*, (Oxford ; New York: Oxford University Press, 2009), 236-242; Pulido, *Vae inventoribus*, 260ff.

³⁴ 34. In *Le choléra d'après le Dr don Jaime Ferran* (Toulouse: Privat, 1885), Duhourcau commented on the main publications on the controversy up to July 1885, to which he had access, apparently, through his exchanges with Ferrán. This seems to be also the case of both Cameron and Boyd, although the former engages in an extensive original discussion of the statistics of the vaccination campaign (citing no source), that the latter partially reproduces: see Cameron, "On Ferran's Anti-Cholera Inoculation," *Proceedings of the Royal Philosophical Society of Glasgow 17*, 1885-86, 1-16; and

Boyd, "Ferrán's Anti-Cholera Vaccination," *Edinburgh Medical Journal*. 35.7, 1890, 639-649. Only Abréu seems to have done some field work: *O medico Ferran e o problema scientifico da vacinação choleric* (Lisboa: Typografia Universal de Thomaz Quintino Antunes, 1885).

³⁵ 35. This was a field mission jointly supported by the University of Cambridge and the Royal Society of London, and its main focus was the identification of the bacilli causing the epidemy. They examined samples of Ferrán's vaccine but did find in them neither Koch's comma bacilli nor any other active principle: C. S. Roy, J. Graham Bron and C. S. Sherrington, "Preliminary Report on the Pathology of Cholera Asiatica (as observed in Spain 1885)" *Proceedings of the Royal Society of London* 41, 1886, 173-181.

³⁶ 36. See Filomeno da Câmara Melo Cabral, "A cólera em Valência e o sistema de profilaxia anti-colérica do Dr. Jaime Ferrán y Clúa" *Revista de estudos livres* 3.4, 1885-1886, 157-216. Edward O. Shakespeare was commissioned in 1885 by the US president Grover Cleveland to prepare a report on cholera, later published as *Report on Cholera in Europe and India* (Washington: Government Printing Office, 1890). Shakespeare visited Ferrán and compiled all the documentation he could gather on his vaccine. Rather than a new assessment, he provided educated commentary on the controversy, defending the quality of the available statistical reports against the objections of the Brouardel commission.

³⁷ 37. For the report, see A. Charrin, J. Albarran, & P. Brouardel, *Rapport sur les essais de vaccination cholérique entrepris en Espagne par M. le Dr Ferran, présenté au ministre du Commerce par MM. P. Brouardel, Charrin et Albarran*. (Paris: G. Masson, 1885) See also Fernández Sanz, 1885, 146; Ferrán y Clúa, *La inoculación preventiva*, 232ff; Pulido, *Vae inventoribus*. Pasteur praised the work of the commission at the Academy (L.Pasteur, "Hommage à L'Académie du Rapport du Dr. Brouardel sur sa mission en Espagne" *C R Hebd Seances Acad Sci CI*, 146, 1885). For other equally skeptical reports from France and Belgium, see Duhourcau, *Le choléra*, 120-130.

³⁸ 38. Local taxes depended on the number of citizens in the census which was an incentive for municipalities to lower the count (Charrin et al., *Rapport*, 926). For a rejoinder to these objections, see Ferrán y Clúa, *La inoculación preventiva*, 247-260.

³⁹ 39. Ferrán y Clúa, *La inoculación preventiva*, 233. According to Boyd ("Ferrán's Anti-Cholera Vaccination", 641) Vulpian, a member of the Bréant jury, would have

claimed: “Je ne savais pas qu'il y avait trois cents médecins dans l'Espagne qui savaient lire et écrire!” To explain the reaction of the, otherwise Francophile, Ferrán and his supporters to the *patronizing* attitude of the French commission, we may recall the 1876 controversy on whether that had been any modern science in Spain. The focal point in this debate was the entry “Espagne” that N. Masson the Morvilliers had prepared for the *Encyclopédie* a century before, claiming that Europe intellectually owed nothing to Spain. Had there been one such contribution, some of the polemicists claimed, why hadn't Europe acknowledged it? See E. & E. García Camarero, eds., *La polémica de la ciencia Española* (Madrid, Alianza, 1970).

⁴⁰ 40. Pulido, *Vae inventoribus*, 362. We should insist that we cannot discard the existence of this prejudice. E.g., in an unpublished letter in French submitted to the Bréant jury, (P.L. Rézard de Wouves, “La question du microbe cholérique”, Dossiers Prix Bréant 1886, candidate 28), criticizes the Brouardel report precisely in terms of its implicit prejudices. Rézard De Wouves, a physician, had been himself advisor to the French Ministries of agriculture and commerce and found Brouardel incompetent to judge the scientific contribution of Ferrán.

⁴¹ 41. V. Sanchís, “Ferrán y el cólera del 85 en Valencia,” *Anales de la Universidad de Valencia*, 25(3), 1951, 44-73, 61.

⁴² 42. For a discussion of the authority of the Academy, we follow M. P. Crosland, *Science under control: the French Academy of Sciences, 1795-1914*. (Cambridge ; New York: Cambridge University Press, 1992).

⁴³ 43. Abréu, *O medico Ferran*, whose testimony we take at face value, since we have not been able to locate many of those assessments.

⁴⁴ 44. E. Maindron, *L'Académie des sciences: Histoire de l'Académie, fondation de l'Institut national, Bonaparte membre de l'Institut national*, (Paris: F. Alcan: 1888).

⁴⁵ 45. M. Crosland & A. Gálvez, “The Emergence of Research Grants within the Prize System of the French Academy of Sciences, 1795-1914,” *Social Studies of Science*, 19(1), 1989, 71-100.

⁴⁶ 46. Académie des sciences, “Programme des Prix Proposés. Médecine et Chirurgie. Prix Bréant,” *C R Hebd Seances Acad Sci CI*, 1887, 1421-1422

⁴⁷ 47. P. Gauja, *L'Académie des sciences de l'Institut de France* (Paris: Gauthier-Villars, 1935) 146-152.

⁴⁸ 48. Crosland, *Science under control*, 98-102; J.E. McClellan, *Science reorganized: Scientific societies in the eighteenth century* (N. York: Columbia University Press, 1985), 258.

⁴⁹ 49. H. Gispert, *Par la science, pour la patrie l'Association française pour l'avancement des sciences, 1872-1914* (Rennes: Presses universitaires de Rennes: 2002).

⁵⁰ 50. Mirko Grmek, "Le concept de maladie," in *Histoire de la pensée médicale en Occident, vol.3*, ed. Mirko Grmek (Paris: Seuil, 1999), 147-167, 157.

⁵¹ 51. As we will see below, in the minutes of the period considered we have found three submissions from Ferrán in July, well past the deadline.

⁵² 52. J.-P. Dedet, *La microbiologie, de ses origines aux maladies émergentes* (Paris: Dunod, 2007), 36-56.

⁵³ 53. L. A. Gosselin, Decision of the Jury, undated, 1 page Dossiers Prix Bréant 1884. Also in *C R Hebd Seances Acad Sci C*, 1884, 529.

⁵⁴ 54. See P. Gauja, *Les fondations de l'Académie des sciences (1881-1915)* (Paris: L'Observatoire d'Abbadia, 1917), 147.

⁵⁵ 55. J. Théodoridès, *Histoire de la rage: cave canem* (Paris: Masson, 1986), 189.

⁵⁶ 56. Gauja, *Les fondations*, 147.

⁵⁷ 57. Here is the list of Ferrán's submissions: (1) "Sur l'action pathogène et prophylactique du bacillus-virgule" (cited on note 22). (2) "Note sur la prophylaxie du choléra", dated in Madrid, 10 July 1885, Dossiers Prix Bréant, 1885, candidate 23; "Sur la prophylaxie du choléra" (cited on note 22) (3) "Nota sobre una vacuna química contra el cólera", dated in Valencia on July 28th 1885, Dossiers Prix Bréant 1885, candidate 23; "Lettre à M. le Secrétaire perpétuel, au sujet du procédé de vaccination contre le choléra. Par M. le Dr. J. Ferrán". Séance du lundi 31 juillet 1885. Mémoires présentés," *C R Hebd Seances Acad Sci CI*, 1885, 367. (4) Statistical sources, Dossiers Prix Bréant, 1885, candidate 23; J. Ferrán y Clúa, *Impreso de colerización Ferrán 1ª serie: Estadísticas de la Inoculación preventiva del cólera morbo asiático* (Valencia: Imprenta

y librería de Ramón Ortega: 1885); this booklet is cited in the *C R Hebd Seances Acad Sci, CI*, 1885, 648.

⁵⁸ 58. E. Fischer, *Biographisches Lexikon der hervorragenden Ärzte der letzten fünfzig Jahre*, Vol. 2 (Berlin-Vienna: Urban & Schwarzenberg, 1993), 807.

⁵⁹ 59. J. Ferrán y Clúa, " Sur l'action pathogène et prophylactique du bacillus-virgule", 31 March 1885.

⁶⁰ 60. E. van Ermegen, from the *Académie Royale de Médecine de Belgique*, and the French bacteriologist P. Gibier had been part of the Belgian and French delegations who had visited Ferrán's laboratory. They read a note on the experiments at the Academy on August 18th 1885 P. Gibier, & E. van Ermengem, "Recherches expérimentales sur le choléra," *C R Hebd Seances Acad Sci CI*, 1885, 470-472.

⁶¹ 61. Ferrán y Clúa, "Note sur la prophylaxie du choléra" (10 July 1885).

⁶² 62. L. Gosselin, *Assessment*, undated, 15 pages, page 2, Dossiers Prix Bréant, 1885, candidate 23.

⁶³ 63. Ferrán y Clúa, "Nota sobre una vacuna química" (28 July 1885).

⁶⁴ 64. Gosselin, *Assessment 1885*, 5

⁶⁵ 65. Ibid.

⁶⁶ 66. A. Sierra y Carbó, *La inoculación anticholérique del doctor Ferrán considerada bajo el punto de vista de la química biológica* (Madrid: Imprenta de Enrique Teodoro: 1885).

⁶⁷ 67. Gibier & van Ermengem, "Recherches expérimentales sur le choléra."

Chantemesse obtained a mention in the 1887 Bréant for his *Recherches sur le bacille typhique* - See Gauja, *Les fondations*, 148. We were not able to find the assessment in the archive (Dossiers Prix Bréant, 1887).

⁶⁸ 68. Gosselin, *Assessment*, undated, 1 page A, Dossiers Prix Bréant 1885, candidate 23. However, in the archive we found no other report as thorough as Gosselin's and no mention of the 100.000 francs award which somehow speaks for the relevance of Ferrán's submission. As a matter of fact, the 100.000 francs were never awarded. As a reviewer suggests, in the early years of vaccinology, Ferrán was not the only one who saw his claims of efficacy denied for methodological sloppiness or lack of proper data.

Almroth Wright's original typhoid vaccine suffered a similar fate: see A. Hardy, "Straight back to barbarism': antityphoid inoculation and the Great War, 1914," *Bulletin of the History of Medicine*, 74(2), 2000, 265-290; J. Williamson, K. Gould & K. Brown, "Richard Pfeiffer's typhoid vaccine and Almroth Wright's claim to priority," *Vaccine* 39(15), 2021, 2074-2079.

⁶⁹ 69. Gosselin apparently had access to data from 7 towns -although he sometimes cites only 6. In the Academy's archive (Dossiers Prix Bréant, 1885, candidate 23) we find five notarial affidavits of the inoculation statistics of Alcira, Benifayó, Catarroja, Chiva and Masanasa. There are no affidavits for Alberique and Cheste, although both are included in Gosselin's calculations.

⁷⁰ 70. The Bréant jury only received the raw data (registrar's certificates) from a sample of 7 towns, and then a booklet with a transcript of the certificates (J. Ferrán y Clúa, *Impreso de colerización Ferrán*, cited in the *C R Hebd Seances Acad Sci*, CI, 1885, 648). It is not clear whether the booklet and the raw data were received at the same time: Gosselin seems to be working with the certificates. In the 1886 book (Ferrán y Clúa, *La inoculación preventiva*), we find instead a collection of records from 28 towns certified by a local authority.

⁷¹ 71. Ferrán and Clúa, *La inoculación preventiva*, 310.

⁷² 72 Gosselin, *Assessment 1885*, D.

⁷³ 73. Ferrán's note was discussed on January 18, 1886 and published on the *C R Hebd Seances Acad Sci*, CII, 1886, 159-60. A.L. Gosselin, *Assessment*, undated, Dossiers Prix Bréant, 1886, candidate 31.

⁷⁴ 74. J. Ferrán and Clúa, "M. Ferrán prie L'Académie de tenir en compte, dans l'examen des recherches effectuées pour la découverte de la vaccine chimique du choléra asiatique, des documents qu'il lui a adressés à diverses reprises et dont il renouvelle l'envoi. Séance du lundi 27 aout 1888. Memoires presentés.," *C R Hebd Seances Acad Sci CVII*, 1888, 454.

⁷⁵ 75. See N. Gamaleïa, "Sur la vaccination préventive du choléra asiatique," *C R Hebd Seances Acad Sci*, CVII, 1888, 432-435. Gamaleïa had been trained in Paris under Pasteur's supervision before assuming the scientific direction of the Bacteriological Institute of Odessa (A.M. Prokhorov, *Great Soviet encyclopedia*, s.v. "N. Gamaleïa")

(New York,: Macmillan, 1973)). He had been an occasional contributor to the sessions at the Academy.

⁷⁶ 76. J. Ferrán y Clúa, "M. Ferrán adresse une série de documents destinés à établir ses droits de priorité à la découverte des vaccins du choléra asiatique. Séance du lundi 22 octobre 1888. Memoires presentés," *C R Hebd Seances Acad Sci, CVII*, 1888, 645.

⁷⁷ 77. In the Ferrán Archive there is a 1888 draft letter addressed to Pasteur in the same terms, although there is no trace of it being sent (Fons Jaume Ferran, C1D160).

⁷⁸ 78. The documents are in the Dossiers Prix Bréant 1888, without reference number

⁷⁹ 79. *C R Hebd Seances Acad Sci CVII*, 1888, 1081.

⁸⁰ 80. They were not considered for any award in the minutes, although their submissions were filed in the same dossier.

⁸¹ 81. E. Roux, "Rapport sur les travaux de M. J. Ferrán," *C R Hebd Seances Acad Sci CXLV*, 1907, 1030-1031.

⁸² 82. Pulido, *Vae inventoribus*, 74.

⁸³ 83. After the Bréant award Roux seems to have had some scientific correspondence with Ferrán: at the Fons Jaume Ferran we find four letters dated on May 15th, 1913 (C8D23); April 14th, 1913 (C8D68); April 20th 1913 (C8D22); January 14th, 1922 (C8D60) and an undated telegram (C7D86). On May 15th, 1913 (C8D23), for instance, Roux addresses Ferrán as "Cher Maître".

⁸⁴ 84. Bornside, "Waldemar Haffkine's cholera vaccines and the Ferran-Haffkine priority dispute," *Journal of the History of Medicine and Allied Sciences*, 37(4), 1982, 399-422.

⁸⁵ 85. López Piñero, *La ciencia en la España del siglo XIX* (Madrid: Marcial Pons:1992), 40.

⁸⁶ 86. Ferrán y Clúa, *La inoculación preventiva*, 232ff.

⁸⁷ 87. Pulido, *Vae inventoribus*, 355-379.

⁸⁸ 88. e.g. V. Huber, "The unification of the globe by disease? The International Sanitary Conferences on Cholera, 1851–1894," *Hist J*, 49(2), 2006, 453-476.

⁸⁹ 89. Fernández Sanz, *1885*, 136ff.

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- ⁹⁰ 90. López Piñero, *Santiago Ramón y Cajal*, p. 182.
- ⁹¹ 91. Fernández Sanz, 1885, 148; Pulido, *Vae inventoribus*, 263.
- ⁹² 92. see, e.g. Sánchez Aldeguer, *Nuevas aportaciones*, 124-126.
- ⁹³ 93. Bornside, "Jaime Ferran".
- ⁹⁴ 94. *Ibid.*, 531.
- ⁹⁵ 95. Alonso et al., "Memoria", 303. Pasteur had made a similar observation in a letter to Ferrán dated on May 23rd, 1885 (Fons Jaume Ferran, C1D76). In "On Ferran's Anti-Cholera Inoculation", Cameron engaged with these objections in these same terms.
- ⁹⁶ 96. The records are preserved, still yet to be catalogued at the Fons Jaume Ferran. There is a published partial version in Ferrán y Clúa, "Impreso" and Ferrán y Clúa, *La inoculación preventiva*.
- ⁹⁷ 97. P. Hauser, *Estudios epidemiológicos relativos á la Etiología y Profilaxis del Cólera basados en estadísticas, hechos y observaciones recogidos durante la epidemia colérica de 1884-85 en España y acompañados de 18 mapas y 25 cuadros epidemiográficos*, (Madrid: Manuel Tello, 1887).
- ⁹⁸ 98. J.P. Vandenbroucke, H.E. Rooda & H. Beukers, "Who made John Snow a hero?", *American Journal of Epidemiology*, 133(10), 1991, 967-973. See also C. Uzcanga-Lacabe, "Una lucha tardía para defender la teoría localista: dos cartas de Hauser a Pettenkofer," *Dynamis*, 33(2), 2013, 485-503.
- ⁹⁹ 99. C. Del Moral, "Importancia de las relaciones sociales en la obra científica de Philipp Hauser," in *Entre Sevilla y Madrid: estudios sobre Hauser y su entorno*, ed. J.L. Carrillo, (Sevilla: Universidad de Sevilla, 1996), 59.
- ¹⁰⁰ 100. *Ibid.*, 60. Hauser was sponsored in his career by the Rothschild family.
- ¹⁰¹ 101. P. Hauser, *Memorias autobiográficas* (Sevilla: Universidad de Sevilla, 1990), 59.
- ¹⁰² 102. P. Hauser, Letter to the Academy of Sciences, dated on 25 February 1888, Dossiers Prix Bréant, 1888, candidate 2. Hauser dedicated *à la mémoire vénérée du professeur Charcot* his *Etudes épidémiologiques. Le choléra en Europe depuis son*

origine jusqu'à nos jours en rapport avec les doctrines courantes relatives à son étiologie et sa prophylaxie (Paris: Société d'Éditions Scientifiques; 1897).

¹⁰³ 103. "Séance du lundi 24 Décembre 1888", *C R Hebd Seances Acad Sci, CVII*, 1888, 1081-1083.

¹⁰⁴ 104. Gauja, *Les fondations*, 147-148.

¹⁰⁵ 105. E. J. Marey, "Sur l'épidémie de choléra: les eaux contaminées et le choléra," *Bulletin de l'Académie de Médecine*, 13, 1884, 1460-1488.

¹⁰⁶ 106. P. Le Gendre, *Charles Bouchard, son oeuvre et son temps* (Paris: Masson et Cie, 1924).

¹⁰⁷ 107. Hauser, Letter to Pettenkofer, December 26th, 1888, *Pettenkoferiana* (II.9, 9 eBU).

¹⁰⁸ 108. Hauser, *Études épidémiologiques. Le choléra en Europe depuis son origine jusqu'à nos jours, en rapport avec les doctrines courantes relatives à son étiologie et à sa prophylaxie: Avec plusieurs cartes et de nombreux tableaux graphiques* (Paris: Soc. d'éditions scientifiques, 1897).

¹⁰⁹ 109. T. Corbella Domenech, "Antecedentes de la enseñanza de estadística en las universidades de Cataluña."

¹¹⁰ 110. *Enciclopedia Universal Ilustrada Europeo-Americana*, s.v. "P. Hauser." (Barcelona: Hijos de J. Espasa, 1888).

¹¹¹ 111. A reviewer suggests that Waldemar Haffkine's 1909 Bréant could have provided another test case about the Academy's attitude regarding statistical data. Born in Russia with French nationality, Haffkine had developed a cholera vaccine that he evaluated in India in 1893 and is now consensually acknowledged as the first effective inoculation -see Bornside, "Waldemar Haffkine's cholera vaccines". Twenty years after Ferrán's initial submission, and a decade after Haffkine's evaluations, the jury was now positive about their contributions. Following the recommendation of E. Roux, reviewer for both Ferrán and Haffkine, awarding 2500 francs to the former in 1907 and 4000 to the latter -Haffkine felt nonetheless overlooked: J. Hanhart, *Haffkine, une esquisse* (Ph.D. Thesis, Université de Lausanne, 2013), p. 194. Still, the Academy cited explicitly the key methodological insight of his statistical studies as a reason for the

award (“Séance du 20 Décembre 1909“, *C R Hebd Seances Acad Sci*, CXLIX, 1909, 1258-1259): the comparison of inoculated and non-inoculated groups of people, living in similar conditions, tabulating his outcomes accordingly and assessing the efficacy according to the between-groups difference in mortality. Haffkine’s evaluation is still considered as a landmark in the history of fair trials: B. Hawgood, “Waldemar Mordecai Haffkine, CIE (1860–1930): prophylactic vaccination against cholera and bubonic plague in British India,” *Journal of Medical Biography*, 15.1 (2007), 9-19. For a similar controversy, see W.C. Summers, "Cholera and plague in India: the bacteriophage inquiry of 1927-1936," *Journal of the History of Medicine and Allied Sciences* 48(3), 1993, 275-301.

¹¹² 112. Hess, "A paper machine", 493.