

The social production of novelty: diphtheria serotherapy, «herald of the new medicine»

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This issue of *Dynamis* presents a collection of articles on the beginnings of a biological treatment: diphtheria serotherapy. This therapy contributed to a decisive change in public and private behaviours towards cases of infectious/contagious disease. The phrase «herald of the new medicine», which appears in the title of this introduction, was used by the Spanish Health Council to describe the treatment of diphtheria by serum taken from the blood of immunised horses, i.e., the Behring-Roux method. This new therapy had been reported to the Council by Antonio Mendoza and Manuel Sanz on their return from official visits to Paris and Berlin in Autumn 1894. The description reflects the perception of novelty, of successful innovation generated by their report. Articles by Gabriel Gachelin and Jonathan Simon, respectively, offer a detailed analysis of the French side of the initial production of serum, while Axel Hüntelmann tells the German side of the same story. Annick Opinel addresses the implications of the new therapy for hospital practice in her account of the construction of the Pasteur Hospital, which was designed to fight against diphtheria.

This introduction aims to show the relevance of these papers to current historiography on the construction of one-cause-medicine, a powerful force in the shaping of health, disease and care in the present world.

Diphtheria appeared in industrial countries between the mid-19th and mid- 20th centuries as an endemic disease with epidemic outbreaks at irregular intervals¹. It has become a fashionable subject of historical

1. BURNET, Macfarlane. *Historia de las enfermedades infecciosas*, Madrid, Alianza Editorial, 1967; CARMICHAEL, Anne. Diphtheria. In: Kenneth F. Kiple (ed.), *The Cambridge world history of hu-*

interest for several reasons. It was the first typically human disease subjected to the entire programme derived from the new bacteriology. Thus a pathogenic germ was established, a biological treatment was developed (serum from hyper-immunised animals), a standard susceptibility test was created (Shick's skin test) and, finally, a vaccine was produced, which was widely employed to curb and almost eradicate diphtheria in Europe and Northern America². A worldwide decline in diphtheria cases of around 70% was recorded between the mid-1970s and the early 1990s. More recently, however, there has been an increased incidence as a skin infection and also as endocarditis, with a case-fatality rate of > 40%³. The collapse of the Soviet Union in the 1990s has led to its re-emergence in Europe refreshing, with incident rates of 0.5-1 per 100,000 in Armenia, Estonia, Lithuania and Uzbekistan and of 27-32 per 100,000 in Russia and Tajikistan, while the case-fatality rate ranges from 2 to 23%⁴.

Diphtheria serotherapy has been described as the crucial link between public excitement about Pasteur's rabies vaccine and the establishment of national campaigns against tuberculosis, sustaining the development of bacteriology-based public health service. This observation, first made in the setting of Germany, has been confirmed by independent studies in other national settings, including Spain⁵. That Emil von Behring (1854-1917), who discovered the antitoxic power of sera from hyper-immunised animals,

man disease, Cambridge, CUP, 1993, 680-683; NEWSHOLME, Arthur. *Epidemic diphtheria: a research on the origin and spread of the disease from an International Standpoint*, s.l., Swan Sonnensch and Co. Ltd, 1898; GOTTSTEIN, Adolf. *Epidemiologische Studien über Diphterie und Scharlach*, Berlin, Springer, 1895; MARCO, Luis. *La difteria en España y en Madrid*, Madrid, Est. Tip. E. Teodoro, 1888.

2. CARMICHAEL, note 1; HARDY, Anne. *The epidemic streets: infectious disease and the rise of preventive medicine 1865-1900*, London, Clarendon Press, 1993, especially pp. 80-109; HAMMONDS, Evelyn M. *Childhood's deadly scourge: the campaign to control diphtheria in New York City, 1880-1930*, Baltimore, The Johns Hopkins University Press, 1999; HOOKER, Claire; BASHFORD, Alison. Diphtheria and Australian public health: bacteriology and its complex applications, c. 1890-1930. *Med. Hist.*, 2002, 46, 41-64; COLGROVE, James. The power of persuasion: Diphtheria immunization, advertising, and the rise of health education. *Public Health Rep.*, 2004, 119, 506-509.
3. GRAEVENITZ, A. von. The changing epidemiology of diphtheria in the past two centuries. *Ann. Ig.*, 2002, 14 (Suppl. 1), 1-5.
4. Data from WHO as of December 2000 [cited 27 February 2007]. Available from: <http://www.who.int/mediacentre/factsheets/fs089/en/>
5. WEINDLING, Paul. From medical research to clinical practice: serum therapy for diphtheria in the 1890s. In: John V. Pickstone (ed.), *Medical innovations in historical perspectives*, New York, St. Martin's Press, 1992, pp. 72-83; HOOKER, BASHFORD, note 2; PORRAS GALLO, María Isabel.

won the first Nobel Prize for Medicine (1901), demonstrates the impact of this innovation and the support that it gained. Its wide use and acceptance were responsible for changes in the standard behaviour of families, doctors and authorities alike towards any suffocating illness in children. It also led to new hospital structures and work dynamics, representing a decisive triumph for medicine based on microbial aetiology. The unleashing of a complex of effects by a single therapeutic innovation fits with general ideas put forward by Bourdelais and Faure on the dissemination of novel practices⁶.

If all of these considerations do not constitute sufficient argument in favour of our compilation, I would presume to claim that these studies make us aware of the profound link among disease, diagnosis and treatment, in other words, interactivity between the development of concepts and practices in medicine similar to that demonstrated in recent research on technologies⁷. The new procedures related to the threat of diphtheria in the second half of the 19th century, before and after the beginnings of bacteriology (e.g., intubation, serotherapy and vaccination) have been studied from a social history perspective of innovation, examining the role of national and professional cultures in their dissemination⁸. This collection explores the same perspective, focusing on the initial development of the complex network used to extend serotherapy and simultaneously the

Antecedentes y creación del Instituto de Sueroterapia, Vacunación y Bacteriología de Alfonso XIII. *Dynamis*, 1998, 18, 81-105.

6. BOURDELAIS, Patrice; FAURE, Olivier (dir.). *Les nouvelles pratiques de santé. Acteurs, objets, logiques sociales (XVIIIe-XXe siècles)*, Paris, Belin, 2005.
7. PICKSTONE, John V. Introduction. In: Pickstone, note 5, pp. 1-16 (14); MEDINA DOMÉNECH, Rosa M.; MENÉNDEZ NAVARRO, Alfredo. Tecnologías médicas en el mundo contemporáneo: una visión histórica desde las periferias. Introducción. *Dynamis*, 2004, 24, 15-26.
8. LIEBENAU, Jonathan M. Public health and the production and use of diphtheria antitoxin in Philadelphia. *Bull. Hist. Med.*, 1987, 61, 216-236; VELLE, K. Arts, Staat en Volksgezondheid: De strijd tegen de difterie in België (1894-1914). *Arch. Belg. Med. Soc.*, 1989, 47, 312-324; HARDY, Anne. Tracheotomy versus intubation: surgical intervention in diphtheria in Europe and the United States, 1825-1930. *Bull. Hist. Med.*, 1992, 66, 536-559; WEINDLING, note 5 and From isolation To therapy: children's hospitals and diphtheria in *Fin de Siècle* Paris, London and Berlin. In: Roger Cooter (ed.), *In the name of the child: health and welfare, 1880-1940*, London, Routledge, 1992, pp.124-145; RODRÍGUEZ-OCAÑA, Esteban. El tratamiento de la difteria en la España de la segunda mitad del siglo diecinueve. *Medicina e Historia*, nº 54 (3ª época), 1994, 5-28; THROM, Carola. *Das Diphtherieserum. Ein neues Therapieprinzip, seine Entwicklung und Markteinführung*, Stuttgart, Wissenschaftliche Verlagsgesellschaft, 1995; KABA, Mariama. La diphthérie à Genève à la fin du XIXe siècle: l'entrée en scène de la bactériologie et l'emploi de la sérothérapie. *Gesnerus*, 2004, 61, 37-56.

laboratory culture throughout the Western world, pinpointing differences between French and German settings.

The following papers report changes linked to the widespread use of serum, starting with its mass production in Germany and in France after mastery of the delicate technique had been achieved and a reliable and regular flow of the product could be guaranteed. In fact, the technical procedures for artificial immunization were developed as an empirical side-effect of research into chemical disinfectants⁹. This was followed by international standardisation of anti-toxic power measurements and profound changes in the pharmaceutical industry (production of antidiphtheric serum was sometimes decisive in the birth of new companies)¹⁰. Widespread use of serum led to changes in hygienic institutions (as shown here in the case study on the Pasteur Institut) as well as the pharmaceutical trade, introducing some new legal regulations and accelerating various changes in the profession. It also contributed to the strengthening of public confidence in scientific medicine, especially in the emerging Children's Medicine, as well as endowing the specialty of Hygiene with a laboratory foundation and generating a network of basic research between the heirs of Pasteur and Koch¹¹. Furthermore, a type of scientific research gained an immediate economic dimension that fuelled the promotion of some experts, whose work was able to sustain large-scale commercial activity. In many cases, researchers who had gained expertise in public laboratories and institutions moved to the private sphere, on their own initiative or recruited by companies. The subsequent shift in the «moral economy» of biological research became a feature that defines present technoscience¹².

9. SIMON, Jonathan. Emil Behring's medical culture: from disinfection to serotherapy. *Med. Hist.*, 2007, 51 (2), 201-218.

10. LIEBENAU, Jonathan. *Medical science and medical industry: the formation of the American pharmaceutical industry*, London/ Baltimore, Macmillan / Johns Hopkins University Press, 1987; TANSEY, E.M. The Wellcome physiological research laboratories 1894-1904: The home office, pharmaceutical firms and animal experiments. *Med. Hist.*, 1989, 33, 1-41. It is a pity that the otherwise overwhelming book by Raúl RODRÍGUEZ NOZAL and Antonio GONZÁLEZ BUENO. *Entre el arte y la técnica. Los orígenes de la fabricación industrial del medicamento* (Madrid, CSIC, 2005) pays no attention to biological medications.

11. WEINDLING, note 5, p. 72.

12. RASMUSSEN, Nicolas. The moral economy of the drug company-medical scientist collaboration in interwar America. *Soc. Stud. Science*, 2004, 34, 161-185. Particularly interesting, in this way, are cases such as those of Emil von Behring and Paul Ehrlich. LINTON, Derek S. *Emil von Behring: infectious disease, immunology, serum therapy*, Philadelphia, American Philosophical

A further theoretical effect brought about by 1891-born serotherapy¹³ was to end discussions on the nosotaxy of a disease whose character and even name remained controversial during the second half of the 19th century. There was debate about the similarities and differences among different types of suffocating angina, diphtheria and croup (a separate disease as defined by the Scotsman Francis Home in 1765, although numerous similar descriptions can be found in the medical literature of the early modern era)¹⁴. The lack of consensus led to national division between supporters and opponents of a united concept of diphtheria¹⁵. Bacteriological diagnosis and especially serotherapy imposed agreement, and modern diphtheria acquired a laboratory identity, a process analysed by Cunningham¹⁶. With this background, it is difficult to establish a history of diphtheria in the *longue durée* based solely on clinical narratives of the time, which were already questioned at the beginning of the 19th century, when it was

Society, 2005; SIMON, note 9; HARDY, Anne. Paul Ehrlich und die Serumproduzenten: Zur Kontrolle des Diphtherieserums in Labor und Fabrik. *Medizinhist. J.*, 2006, 41, 51-84. In Spain, and waiting for deeper studies on the technical personnel of the National Hygiene Institute, who created THIF, a firm producing biological medicaments which merged in 1929 with IBYS, the best known example is provided by Jaime Ferrán's life, see RODRÍGUEZ-OCAÑA, E. Ferrán y Clúa, Jaime. In: W. F. Bynum & Helen Bynum (eds.), *Dictionary of medical biography*, Westport,CT /London, Greenwood Press, 2007, vol. 2, pp. 486-488.

13. First documented case of serotherapy occurred in 1891, managed by Behring and Wernicke. OEDINGEN, Christina; STAERK Joseph W. First cure for diphtheria by antitoxin as early as 1891. *Annals of Science*, 1997, 54, 607-610.
14. Spanish authors described the disease named *garrotillo* (from the suffocation caused by the common device —*garrote*— used for executions) in the 16th and 17th centuries, AMORÓS SEBASTIÁ, L.I. et al. La difteria y los médicos españoles del Renacimiento. *Acta Otorrinolaringol. Esp.*, 2002, 53, 146-150.
15. Curiously, experts from the past and modern ones do not agree upon this divide. SANNÉ, Albert. Diphthérie. In: A. Dechambre (ed.), *Dictionnaire encyclopédique des sciences médicales*, Paris, P. Asselin/G. Masson, 1884, vol. 29, pp. 548-721 (556-557), put together French and American doctors and draws German and British as supporters of the division between croup and diphtheria, while HARDY (note 2, p. 85) joins all Anglosaxons into a single group to oppose French unitarian doctrine. In Spain, even though both names were employed, unitarianism prevailed, RODRÍGUEZ-OCAÑA, note 8. See GUTIÉRREZ RODILLA, Bertha M. Errores conceptuales y sus repercusiones terminológicas: el caso del «croup» en la historia de la difteria. In: Fernández García; Joaquín; Castillo Ojugas, Antonio (eds.), *La medicina popular española. Trabajos dedicados al Dr. D. Antonio Castillo de Lucas en el Centenario de su nacimiento*. Oviedo: ASEMEYA, 1998, for a normativistic perspective of the same debate.
16. CUNNINGHAM, Andrew. La transformación de la peste: El laboratorio y la identidad de las enfermedades infecciosas. *Dynamis*, 1991, 11, 27-71; CUNNINGHAM, A.; WILLIAMS, Perry (eds). *The laboratory revolution in medicine*, Cambridge, Cambridge University Press, 1992.

reported that «in none of them can we found all the appropriate features [for diphtheria]»¹⁷. However, new DNA technology has allowed laboratory exploration of past times, and bacteria from genus *Corynebacterium*, with no more precision, were recently detected in human remains from Ancient Egypt (c. 1550-1080 aC)¹⁸.

A germ aetiology for diphtheria evolved from studies by Klebs (finding of *Corynebacterium diphtheriae*, 1883), Löffler (experimental reproduction of the disease in animals, 1884) and Roux and Yersin (discovery of endotoxin, 1888), although it was not accepted before the large-scale application of serotherapy started in 1894-95. Microbes was not included among the following causes of diphtheria described in a leaflet distributed to the public by the Madrid Health Council in 1888 (Instrucciones populares para prevenir el desarrollo y propagación de la difteria): «[...] bad housing, scarce food, lack of cleanliness, lack of shelter in cold and humid seasons and in general the regrettable abandonment of hygienic commandments [...]». Nascent bacteriology had to fight on two fronts at the same time, against the environmentalism of hygienists and against the traditions of clinicians.

This new biological therapy helped to settle some other medical disputes around diphtheria. General and local antiphlogistic measures were used in therapy, but this pattern changed in the second half of the 19th century. Around 1880, a common treatment prescription included emetics and tonics, local cauterization with silver nitrate and iron perchloride, brushstrokes with potassium permanganate and the tearing out the false membranes¹⁹. Tracheotomy, as recommended by Trousseau, was used to combat the feared condition of asphyxia²⁰. A less dramatic alternative to this operation was intubation, a procedure that had been used for several pathological conditions since 1815. Designated *tubage*, it was applied to treat diphtheric asphyxia in the mid-19th century by French specialists,

17. Croup, in *Diccionario de ciencias médicas*, Madrid, Imp. Mateo Repullés, 1822, vol. 8, pp. 326-363 (327).

18. ZINK, Albert *et al.* *Corynebacterium* in Ancient Egypt. *Med. Hist.*, 2001, 45, 267-272.

19. CADIER. *Manual de laringoscopia y laringología*. [Being the summary of a series of lectures given at the École Pratique of the School of Medicine in 1878 and 1879] translated from the last French edition [*Manuel de laryngoscopie et de laryngologie*, Paris, Delahaye, 1880], Madrid, Romero, 1881, pp. 101-102. See HARDY, note 8, pp. 544-545.

20. Trousseau presented his first experiences in a series of articles appeared in 1833 and 1834 on the *Journal des Connaissances médicochirurgicales*, which were later summarised on the *Encyclographie des Sciences médicales. Répertoire Général des Sciences Médicales au XIXe siècle...* (Bruxelles, Société Belge de Librairie, 1841, vol. 9, pp. 191-196: «De la trachéotomie dans le croup»).

notably Eugène Bouchut (1818-1891), although he used it fewer than half-a-dozen times before 1879²¹. Tracheotomy remained the operation of choice until the introduction of technical improvements by the American physician Joseph O'Dwyer (1841-1898) between 1885 and 1887, after which intubation became a preferred approach, especially in the USA²². Hardy (1992) found a strong reason for this shift in the non-surgical nature of the intervention, especially well-suited to the search for legitimization by the emerging specialists in Children's Medicine.

Although both operations initially resolved the critical condition, i.e., re-opening the airway, this success could be short-lived, since this purely mechanical treatment did not reverse the infection. According to the French and Scottish literature, survival rates for all operated patients were 25-30% in around 1870²³. Between 1870 and 1889, the survival rate for tracheotomies at two hospitals in Geneva was 49-53%, decreasing to 26% in 1890-91²⁴. After serotherapy became available, these figures improved, with a 50% reduction in mortality rates. At the beginning of the 20th century, it was reported that «[...] a great deal of practitioners who have practiced both operations agree nowadays that intubation is the operation of choice and tracheotomy that of necessity»²⁵.

Serotherapy was not without drawbacks, and its massive use revealed some hazards. Thus, anaphylaxis was described in 1902. Earlier proposals by Roux and others for the prophylactic use of the serum were rapidly forgotten. In 1896, major controversy arose in Germany over the death of Ernst Langerhans, the 8-yr-old son of a highly regarded physician, after the preventive injection of diphtheric serum²⁶.

Nevertheless, diphtheria disappeared from the front line of the causes of mortality in industrial countries during the 20th century. Thus, specific diphtheria mortality in Belgium fell from a rate of 135.90 per 100.000 in

21. BOUCHUT, E. *Tratado práctico de las enfermedades de los recién nacidos y de los niños de pecho y de la segunda infancia*, 2ª ed., Madrid, Carlos Bailly-Baillière, 1879, p. 358.

22. See works by HARDY and RODRÍGUEZ-OCAÑA quoted in note 8.

23. HARDY, note 8, p. 539.

24. KABA, note 8, p. 45.

25. RODRÍGUEZ VARGAS, Alfredo. *Intubación de la laringe en el niño y en el adulto*, Valladolid, Imp. y Lib. de J. Montero, 1908, p. 185; on recorded mortality following tracheotomy, p. 202. The original statement comes from the French neurologist and expert in infectious diseases Louis Landouzy (1845-1917), as quoted by HARDY, note 8, p. 550.

26. HÜNTELMANN, Axel. Das Diphtherie- Serum und der Fall Langerhans. *Med. Ges. Gesch.*, 2005, 24, 71-104.

1861-64 to 27.10 in 1896-1900, 12.17 in 1911-13 and 5.24 in 1933-35²⁷. In Spain, this mortality fell by 74.6% between 1911 and 1930²⁸. The fall is usually explained by the massive use of effective methods of immunological defence: first serotherapy, starting in autumn 1894, and then the vaccine, from 1923 onwards. However, there are reasons to doubt the equation that links the use of serotherapy with the reduction in diphtheria, primarily because of historic variations in estimates of the numbers involved. International research carried out by Arthur Newsholme (1857-1943) in 1898 concluded that diphtheria was present in all great capitals and populous cities in the world but that there were continuous fluctuations in specific mortality rates. Hardy attributes this to the different pathogenic strengths of the three different strains of *C. diphtheriae* that are harmful to humans and she points out that the birth of serotherapy coincided with a cycle of low-intensity diphtheria, which might have produced an overvaluation of the benefits of the new treatment²⁹. Contemporary studies show the co-existence of typically endemic strains with epidemic clones and of toxogenic with non-toxogenic strains³⁰.

It is indisputable that a rapid consensus was achieved on serotherapy and that it was widely used. A survey by the American Pediatric Society (1896 and 1897) showed that serotherapy reduced overall diphtheria mortality to 13%, while its use from the first day of the disease illness yielded a mortality rate of only 4.9%³¹. In 1901, however, the prominent Austrian paediatrician Ludwig Unger (1848-1923) stated that serotherapy was too weak a remedy to produce a profound change in the situation and that mortality had reached historical maximums in some places, e.g., Trieste and Saint Petersburg³². Nevertheless, serotherapy was supported by a number

27. VELLE, K. Arts, Staat en Volksgezondheid: De strijd tegen de difterie in België (1894-1914) *Arch. Belg. Med. Soc.*, 1989, 47, 312-324 (318).

28. PASCUA, Marcelino. *Mortalidad específica en España. II Mortalidad por sexos, grupos de edades y causas en el periodo 1911-1930*. Madrid, Publicaciones oficiales de la Comisión Permanente de Investigaciones Sanitarias, Dirección General de Sanidad, 1935, pp. 59-61 and tables 24 and 25.

29. HARDY, notes 2 and 8.

30. GRAEVENITZ, note 3.

31. MARKS, Harry M. «Until the sun of science (...) the true Apollo of medicine has risen»: Collective Investigation in Britain and America, 1880-1910. *Med. Hist.*, 2006, 50, 147-166 (p. 160).

32. UNGER, Ludwig. *Tratado de enfermedades de los niños*, Barcelona, J. Espasa [traslación of *Lehrbuch der Kinderkrankheiten in kurzgefasster systematischer Darstellung zum Gebrauche für Studierende und Aerzte*, Leipzig/Wien, F. Deuticke, 3. Aufl. 1901], p. 611.

of statistical studies, e.g., by Victor Chary [*La mortalité par diphtérie en Europe, avant et après l'application de la sérothérapie; étude statistique*, Paris, 1900] and Ernst Marx [*Die experimentelle Diagnostik, Serumtherapie und Prophylaxe der Infektionskrankheiten*, Berlin, A. Hirschwald, 1902]. On the other hand, the influential practitioner Antonin-Bernard-Jean Marfan (1858-1942), himself in favour of serum, also cited other factors in his epidemiological explanations and, in 1904 he related the lower mortality rate to a lower incidence³³.

For a variety of reasons, a greater consensus developed on the therapeutic usage of serum as the 20th century proceeded. Thus, sera were standardised (some English sera were known to lack antitoxic power in comparison with continental European products), allowing physicians and pharmacists to predict the antitoxic power of each phial³⁴. There next followed attempts to standardise indications for amounts of serum and for the method and timing of its administration, a task that took decades. Nevertheless, subcutaneous injection, deemed the least efficient way to administer the serum, was still being used by most physicians in 1915³⁵. Other procedures that were modified included the asepsis of injections and laboratory diagnosis. In many places, e.g., New York, Philadelphia and Paris, health services developed a flexible scheme that allowed the rapid collection of samples and the fast return of a diagnosis to doctors *via* the pharmacy or even *via* police stations. However, in Spain and some other countries, obtaining a quick bacteriological diagnosis was still unlikely in most cases in 1920, because of the lack of laboratory facilities and communication difficulties, with a complete absence of any relevant official provision³⁶.

The popular acceptance of serum was encouraged by access to an abundant supply, mainly thanks to charities, as Mariama Kaba shows in Geneva, and government subsidies. A good proof of the popularity of the new therapy emerged during the devastating influenza pandemic in 1918-1919. The public demanded from the authorities a change in public patterns of intervention, beyond disinfection and isolation measures to a

33. Quote of Marfan as of decembre 1904 *In*: STATISTIQUE de la diphtérie 1903-1904. *Annales d'hygiène publique et de médecine légale*, 1905, sér. 4, n°4, 359.

34. LIEBENAU, note 8, p. 233; HARDY, note 12.

35. Way defended by LLORENTE, Vicente. *Difteria y su curación. Bases en que descansa la acertada aplicación de la Seroterapia*. Madrid, Suc. Rivadeneyra, 1914.

36. MURILLO PALACIOS, Francisco. *El suero antidiftérico*, Madrid, Calpe, 1920.

wide use of sera and at a secondary level, vaccines. The use of antidiphtheric serum in Spain was so high that the Home Ministry had to order mayors and physicians to restrict the therapy so that reserves could be maintained for specific cases³⁷.

Articles in the present collection address the constitution of this new model of anti-infectious practices. Thus, the relevance of basic German-French research to serology is described. Instead of depicting confrontation, as occurred during initial bacteriology investigation into anti-anthrax and anti-rabies vaccine, Gabriel Gachelin reports the growing standardization of techniques and procedures and the formation of an exchange network among researchers and institutions in the two countries.

Annick Oppinel reports on the broad fight against diphtheria and the role of serotherapy. As a result of Roux's connections with Joseph Grancher (1843-1907), head of the infectious disease department of the Hôpital des Enfants-Malades, he was able to incorporate basic elements into the design of the Pasteur Hospital for meeting any type of contingency, including isolation and disinfection procedures. It should not be forgotten that sera were initially and most widely used in hospitals, which saw patients at earlier stages of the disease. As a result, they obtained better results and were able to improve their image as curative establishments. As Opinel shows, the new serum was linked in a beneficial way to new hospital design, new structures and routines, which were later applied to any transmissible disease.

Axel Hüntelmann and Jonathan Simon both study the industrial production and legal regulation of serum in the two pioneer countries. Cultural, social and political differences between the nations are revealed by their distinct regulation road maps and production and sales agents, and by the different instruments applied by the state to govern its use. On the German side, a strong relationship among science, industry and the state is highlighted, such that all obtain important benefits: substantial contracts and careers for researchers, therapeutic products with wide acceptance and a guaranteed sale, and assurances about the control of health risks to the population. On the French side, Simon underlines the charitable image of the Institut Pasteur, thanks to the large profits generated by their discovery

37. RODRÍGUEZ-OCAÑA, Esteban. La Grip a Barcelona. Un greu problema esporàdic de salut pública. Epidèmies de 1889-90 i 1918-19. In: Antoni Roca (ed.), *1891-1991. Cent anys de Salut Pública a Barcelona*, Barcelona, Institut Municipal de la Salut, 1991, pp. 131-156 (150).

of the serum. As practically the only repository of new knowledge on bacteriology and immunology, it attained special status within the French health system. Simon elegantly dissects features peculiar to French administration and legislation in relation to this innovation and the place of its birth.

Taken together, these papers draw our attention to the complexity of innovations while improving our knowledge of the industrial dimension of basic biological sciences and showing the relevance of the local setting in which they are developed and disseminated. I believe that they make a good fit with recent studies on social defence against diphtheria and contribute useful suggestions for this line of research, which indeed would notably improve when including the investigation of perceptions of different publics. ■

