

Professor Sergi Erill Sáez (1938-2020): physician, pharmacologist, teacher, researcher, science communicator, and manager*

Fèlix Bosch^{1#}, Patrick du Souich², and Josep-Eladi Baños³

¹Fundació Dr. Antoni Esteve, Barcelona. ²Département de pharmacologie, Faculté de médecine, Université de Montréal. ³Facultat de Medicina. Universitat de Vic-UCC.

#Correspondence: Fèlix Bosch. Fundació Dr. Antoni Esteve. Passeig Zona Franca, 109. 08038 Barcelona (Catalonia, Spain). Telephone (+34) 934 335 320. fbosch@esteve.org

****The original article has been published in Catalan, with the following reference and link:*** Bosch F, du Souich P, Baños JE. Professor Sergi Erill Sáez (1938-2020): metge farmacòleg, docent, investigador, divulgador i gestor de la ciència. *Annals de Medicina*. 2020;103:92-96. http://annals.academia.cat/view_document.php?tpd=2&i=14779

Introduction

Sergi, as he asked everyone to call him, was loved and respected in the scientific community in his roles as a specialist in internal medicine, pharmacologist, professor, researcher, science communicator, and manager, and above all as a human being. For those of us who had the good fortune of working closely with him, he was a paragon, a mentor, and a friend—a warm person who was always ready and willing to help and support those around him. Unaffectedly intelligent and cultured, he was endowed with a prodigious memory. He was known for his exquisitely respectful treatment of all. Sergi valued people as individuals, regardless of their degrees, positions, or titles. He was constant and exemplary in everything he did; his great capacity for work and commitment were evident in every project he undertook.

Sergi Erill's professional and scientific career attests to his extraordinary capacity to learn, memorize, synthesize, apply, and teach a wide range of materials. His dual training in internal medicine and pharmacology (both basic and clinical) enabled him to translate ideas from basic research to medical care. Without his contributions, pharmacology in general and clinical pharmacology in particular in Spain would have been very different. After an extensive academic career, Sergi agreed to take the helm at the Dr. Antoni Esteve Foundation out of appreciation and respect for the family of his admired friend, Antoni Esteve i Subirana. From this position, Sergi continued to contribute to the different branches of pharmacology and to science in general.

Education

Sergi Erill was born in Barcelona on October 12, 1938, at the height of the Spanish Civil War. He studied at the *Lycée Français* and went on to earn a degree in medicine at the University of Barcelona in 1963. Four years later, he was awarded a PhD for his thesis describing a new technique for detecting antibodies under the direction of Agustí Pedro i Pons, Chair of Internal Medicine [1]. The same year he was granted a *Merck International Fellowship in Clinical Pharmacology* (1967), which allowed him to start training in clinical pharmacology in the United States, first at the University of Kansas with Daniel Azarnoff (1967) and then at the Department of Pharmacology at the University of Michigan (1968-69) with Edward A. Carr and Edward F. Domino. He returned to Catalonia and was certified in internal medicine (1970) and clinical pharmacology (1983). His training in basic and clinical pharmacology combined with his training as a clinician enabled him to develop a wide, transversal vision of medicine and therapeutics. This unique background, together with his experience and international contacts in the field of clinical pharmacology, endowed him with a singular profile among contemporary pharmacologists.

Teaching

Sergi was always very interested in teaching. He started teaching even before he graduated from medical school, in 1962, when he was an intern under Francisco García-Valdecasas, the Chair of Pharmacology at the University of Barcelona's School of Medicine. From 1963 through 1967, he was an assistant teacher in the laboratory classes under the Chair of Clinical Medicine and Pathology, Agustí Pedro i Pons. He continued teaching in the United States, working at the University of Michigan as a research scholar in pharmacology and a teaching associate in internal medicine (1968-69). On his return to Catalonia, he obtained a position as an interim associate professor of physiology (1969-70) and as a tenured associate professor of pharmacology and clinical therapeutics (1971-76) at the Autonomous University of Barcelona's (UAB) School of Medicine. Under Josep Laporte, Chair of Pharmacology, he shared his academic activity with other pharmacologists, such as Jesús García Sevilla, Patrick du Souich, Joan-Ramon Laporte, and Jordi Camí. During this period, Sergi Erill helped consolidate clinical pharmacology in our country, participating in the organization of specific doctoral courses and writing different chapters of the respected Spanish series *Avances en Terapéutica* [2]. In 1976 he attained the Chair of Pharmacology at the University of the Basque Country, where he lived until 1979, when he moved to the University of Granada, where he held the Chair of Pharmacology until 1983. Between 1983 and 1998, back in Barcelona, he combined directing the Dr. Antoni Esteve Foundation with teaching as a professor of pharmacology at the University of Montreal. His wisdom, kindness, and humility made him an excellent supervisor of both undergraduate and graduate students.

Related to his teaching activity and also to his role in managing science, Sergi Erill served as president of the Spanish Association of Pharmacologists from 1982 to 1986, which, in keeping with the times, during the last year of his presidency changed its name to the Spanish Society of Pharmacology (*Sociedad Española de Farmacología*)

During this period he promoted the first symposium about teaching in pharmacology, which was followed in 1999 with the first symposium about innovation in teaching, held in Valencia, the creation of study group focused on teaching and training in pharmacology two years later, and finally a session dedicated to teaching in the Society's congresses, an initiative that would go on for many years. Sergi maintained this interest in education when he was the director of the Dr. Antoni Esteve Foundation, where he started a line of training courses in areas that had not been covered by other institutions. The first of these, a seminar on the workings of clinical research ethics committees, took place in 2001, and went on for seven more editions. These training activities would become one of the Foundation's most important areas of action.

Research

Sergi Erill's training in pharmacology and clinical medicine, together with his capacity and vocation as a teacher, were complemented with many important contributions to research. He formed part of the so-called *Catalan school of pharmacology*, which occupied the chairs at many universities all over Spain. His vision of the discipline considered the practical application of medication in humans with great interest, and he authored the chapter about clinical trials in the innovative book *Bases farmacológicas de la terapéutica medicamentosa* [3], published in 1969, when the concept of these therapeutics was little known in our country. In fact, Sergi returned to Barcelona in 1969 with the idea of setting up a clinical pharmacology department despite the difficulties of doing so when this medical specialty did not yet exist in Spain. His article "Clinical pharmacology in Spain" [4], published in the journal *Clinical Pharmacology & Therapeutics*, lays out his concerns about the need to develop the discipline in Spain. When he became an associate professor at the UAB and Hospital de la Santa Creu i Sant Pau, he managed to organize a team of physicians committed to clinical research. He analyzed the use of medications in Spain, such as chloramphenicol [5], evaluated physicians' knowledge of medications [6], and assessed physicians' perceptions of antibiotics [7].

In the early 1970s, Sergi Erill undertook various projects related to drugs' binding to plasma proteins and acetylation. The methodology of studying the binding of drugs to proteins in humans was a significant problem that Sergi elegantly solved by using the natural filtering process of the salivary glands [8]. He also demonstrated that renal, liver, or respiratory failure, as well as multiple myeloma or diabetes, could modify the binding of acidic and basic drugs to plasma proteins [9-13]. One of his most important contributions was to demonstrate that the binding of acidic drugs to albumin decreases during renal failure due to the carbamylation of the binding site (14). The vast research program about drug binding to proteins also included studies about drug interactions that affected binding [15-17] and the repercussions of changes in binding on the dynamics of the drug [18-20].

Another line of research, based on previous studies, discovered that isoniazid was acetylated according to a bimodal genetic polymorphism; in other words, there are fast and slow acetylators. Years later, it was shown that other drugs, such as dapsone and sulfamethazine, are also acetylated in a bimodal fashion. Sergi Erill formulated the hypothesis that the elimination of procainamide by acetylation occurred bimodally and that different diseases modified the rate of acetylation. First, he demonstrated that 50% of healthy subjects were fast acetylators of procainamide and 50% were slow acetylators

[21-22]. Then he showed how liver failure [23], heart failure, renal failure, and chronic obstructive pulmonary disease affected the speed of acetylation of procainamide [24]. In most of the situations studied, there was an inflammatory reaction, although in animal models this reaction did not seem to be responsible for slowing the rate of acetylation [25]. Renal failure also decreased the speed of the two reactions of hydrolysis, the formation of *p*-aminobenzoic acid, a metabolite of procainamide and the hydrolysis of procaine, and this effect seemed to be independent of the carbamylation of plasma esterase [26]. Finally, in an article published in *Science*, Sergi Erill proposed extending the patents of drugs indicated for tropical diseases to facilitate their availability in areas where there were shortages [27].

Sergi Erill also showed great interest in the conceptualization of pharmacology and in understanding how it developed as a scientific discipline. One noteworthy contribution in this direction was his idea to create the collection “Pharmacotherapy Revisited”, which is published by the Foundation. This is a collection of books that comprise facsimiles of the documents that have played a leading role in the development of the different branches of the medical specialty, selected by experts in the different disciplines. Sergi Erill himself was the editor of two books in the series. The first, *Clinical Pharmacology through the Pen of Louis Lasagna* [28], compiled the most important articles by one of the founders of clinical pharmacology, whom Sergi deeply admired. The second, *From Clinical Research to Clinical Pharmacology* [29], showed readers the development of clinical pharmacology through its main proponents, starting with Harry Gold, who gave the discipline its name.

Sergi never stopped writing articles, producing more than 120 in total, and publishing in top-tier science journals. He also contributed more than 140 other texts, including books, book chapters, and monographs. Moreover, he directed ten doctoral theses and was a member of the editorial boards of scientific journals such as *Clinical Pharmacology Research*, *Drugs and Therapeutics Perspectives*, *Journal of Clinical Epidemiology*, and *Pharmacology and Toxicology*.

Dr. Antoni Esteve Foundation

The Dr. Antoni Esteve Foundation was one of Sergi’s greatest works and one of those he took great pride in. The Esteve family created the Foundation to honor the memory of Antoni Esteve i Subirana four years after his death. The Foundation’s main mission, then and now, has been to stimulate progress in pharmacotherapy through multidisciplinary scientific communication and debate. The friendship and trust between the Esteve family and Sergi Erill led them to propose that he direct the Foundation. Sergi accepted the challenge of becoming the founding director of this institution, and from this position he promoted hundreds of initiatives through the years. He always explained that he conceptualized the Foundation along the lines expressed by the eminent economist Lord William Henry Beveridge’s in his characterization of the CIBA Foundation, constituted in the United Kingdom in 1949, “not a laboratory for mixing compounds, but a laboratory for mixing scientists [30]”. Despite the differences between the two institutions, this foundational idea also guided Sergi Erill in building and growing the Dr. Antoni Esteve Foundation during its 37 years of existence [31].

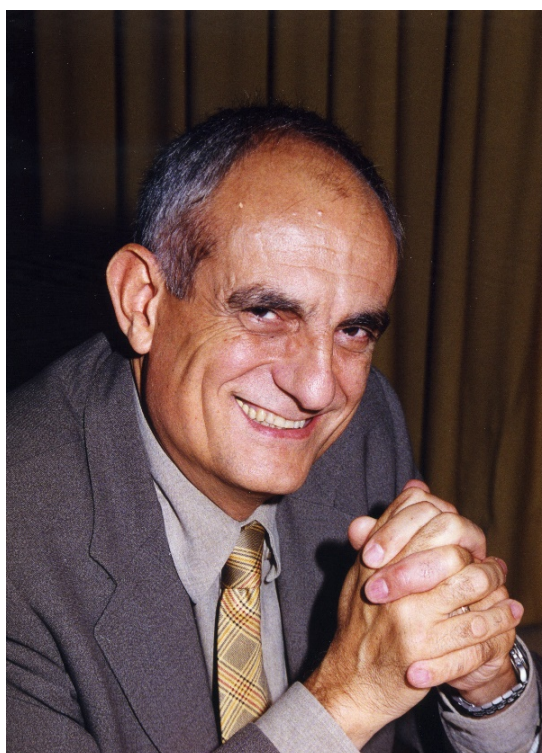


Figure 1. Sergi Erill during an act that he organized through the Dr. Antoni Esteve Foundation in 1999.

The Dr. Antoni Esteve Foundation enabled Sergi Erill to put many of his ideas about pharmacotherapy and scientific communication into practice. His training and international experience were fundamental in enabling him to set up, lead, and manage this institution (**Figure 1**). Among the many initiatives he impelled were national and international conferences and meetings, research prizes, training courses, and publications—all of which can be consulted on the Foundation’s website [32].

In an article published in *Annals de Medicina* (33), Sergi Erill wrote how he felt about his role at the Foundation. Although he was grateful for the opportunity to create and develop the institution, he continued to doubt whether everything that was done could ever be sufficient to honor the memory of Dr. Antoni Esteve i Subirana, despite his satisfaction with the growth in the Foundation’s activity and renown. He stressed how we should all be grateful for the family’s generosity in promoting a Foundation that has benefited society so much.

Science communication and other activities

Together with Vladimir de Semir, Sergi Erill was a driving force behind the first international symposium on science journalism held in Spain. This act in Barcelona in 1990 was one of the seeds from which the Catalan Association of Scientific Communication would grow. This symposium led to the publication of a monograph with an introduction by Sergi Erill (34). Sergi’s special skills and interest in scientific

communication are evident in the many articles he published in the daily press as well as his column “Jabs & Jibes” in *The Lancet* [35-38]. Along these lines, he also published several books to bring science to the people. For example, *Els medicaments i jo (Medicines and me)* [39] taught young children about how different drugs work. His last book, *La ciència oculta (Hidden science)* [40], explained the stories of 15 women who made landmark discoveries in science (**Figure 2**). His commitment to shining light on women scientists was recognized by the *Asociación de Mujeres Investigadoras y Tecnólogas (Association of Women Researchers and Technologists)*, which made him an honorable member in 2012. Sergi Erill also participated in the elaboration of the books *Vocabulari mèdic (Medical vocabulary, in Catalan)* [41] and the *Diccionari de recerca clínica de medicaments (Dictionary of clinical research into drugs, also in Catalan)*[42].

In addition to his role as the president of the Spanish Society of Pharmacology, Sergi Erill served in many academic and professional roles. He was the president of the National Commission on Clinical Pharmacology (1978-81), a World Health Organization expert for the evaluation of drugs (1983-92), a member of the Advisory Board of the Juan March Foundation (1986-88), the president of the National Commission for Pharmacovigilance in Spain (1987-88), the scientific director of Dr. Esteve Laboratories (1989-2003), and a member of the University of Barcelona’s Bioethics Commission and a professor in the master’s program in bioethics and law (1996-2020), among other positions. He was also a member of the International Union of Basic and Clinical Pharmacology’s selection committee from 2006 to 2010. He was always open to accepting responsibility in challenging roles that provided opportunities to contribute, yet he was totally uninterested in awards and recognition.

On February 29, Sergi Erill’s excellent career and exemplary life came to an end. We share his family’s loss and write this simple homage on behalf of all of those who were fortunate to share years, days, or even moments with Professor Sergi Erill Sáez, a great professional, teacher, and researcher, and above all, a great human being who earned our respect and admiration and will forever hold our esteem.



Figure 2. Sergi Erill presenting his last book, *La ciència oculta (Hidden science)*, on November 16, 2017 in Barcelona (left) and on November 20 in Madrid (right, with Pilar Tigeras).

Acknowledgments

The authors thank the Erill family for reviewing the text, Marta Pagans for editing the original, Catalan version of this text, and John Giba for the English translation.

References

1. Erill S. Contribución al estudio de los anticuerpos antiglobulina gamma: desarrollo de una técnica original de detección de anticuerpos por aglutinación de partículas de carbón revestidas de antígeno. Doctoral thesis. Barcelona: University of Barcelona, 1967.
2. Laporte J, Salvà JA, editors. Avances en terapéutica. Different volumes published in Barcelona by Salvat between 1970 and 1992.
3. Valdecasas FG, Laporte J, Salvà JA, Cuenca E, Esplugues J, Bartolomé M, Forn J, Jané F, Brugger A, Erill S, Rodríguez L. Bases farmacológicas de la terapéutica medicamentosa. Barcelona: Salvat Editores, 1969.
4. Erill S. Clinical pharmacology in Spain. *Clin Pharmacol Ther.* 1974;16:597-604.
5. Erill S, du Souich P, García Sevilla JA. Chloramphenicol-containing drugs. A report from Spain. *J Clin Pharmacol.* 1975;15:401-4.
6. Laporte J, du Souich P, Erill S. Conocimiento por parte del médico de la composición y propiedades de las especialidades farmacéuticas más prescritas. *Rev Clin Esp.* 1976;140:269-74.
7. Gómez J, Erill S. Image of systemic antimicrobial agents as perceived by physicians in a 900 bed hospital. *Eur J Clin Pharmacol.* 1979;15:127-32.
8. Pérez-Mateo M, Erill S, Cabezas R. Blood and saliva salicylate measurement in the monitoring of salicylate therapy. *Int J Clin Pharmacol Biopharm.* 1977;15:113-5.
9. Pérez-Mateo M, Erill S. Protein binding of salicylate and quinidine in plasma from patients with renal failure, chronic liver disease and chronic respiratory insufficiency. *Eur J Clin Pharmacol.* 1977;11:225-31.
10. Carlos R, Calvo R, Erill S. Plasma protein binding of etomidate in patients with renal failure or hepatic cirrhosis. *Clin Pharmacokinet.* 1979;4:144-8.
11. Pérez-Mateo M, Erill S. Plasma protein binding of salicylate and quinidine in patients with myeloma. *Int J Clin Pharmacol Biopharm.* 1979;17:168-70.
12. Ruiz-Cabello F, Erill S. Abnormal serum protein binding of acidic drugs in diabetes mellitus. *Clin Pharmacol Ther.* 1984;36:691-5.
13. Guerrero J, García-Morillas M, Gil-Extremera B, Erill S. Serum protein binding of sulfisoxazole and diazepam in patients with chronic obstructive pulmonary disease. *Int J Clin Pharmacol Ther Toxicol.* 1987;25:255-8.
14. Erill S, Calvo R, Carlos R. Plasma protein carbamylation and decreased acidic drug protein binding in uremia. *Clin Pharmacol Ther.* 1980;27:612-8.
15. Calvo R, Carlos R, Erill S. Effects of carbamylation of plasma proteins and competitive drugs displacers in uremia. *Pharmacology.* 1982;24:248-52.
16. Erill S, du Souich P, Courteau H. Carbamylation of proteins and sulfacetamide free fraction in serum in experimentally-induced high blood urea states. *Res Commun Chem Pathol Pharmacol.* 1985;50:45-56.

17. Fernández MC, Erill S, Lucena MI, Pita E, Pérez-Alfárez N. Serum protein binding of tolbutamide in patients treated with antiepileptic drugs. *Clin Pharmacokinet.* 1985;10:451-5.
18. Calvo R, Carlos R, Erill S. Differential effects of valproic acid on the serum protein binding of lorazepam and diazepam. *Int J Clin Pharmacol Res.* 1986;6:213-5.
19. du Souich P, Calvo R, Erill S. Effects of cefotaxime on the serum protein binding of sulfisoxazole. *Biopharm Drug Dispos.* 1990;11:371-9.
20. Martínez Jordá M, Aguirre C, Calvo R, Rodríguez Sasiain JM, Erill S. Decrease in penbutolol central response as caused by changes in its serum protein binding. *J Pharm Pharmacol.* 1990;42:164-6.
21. du Souich P, Verges J, Erill S. Plasma protein binding and pharmacological response. *Clin Pharmacokinet.* 1993;24:435-40.
22. Du Souich P, Erill S. Patterns of acetylation of procainamide and procainamide-derived p-aminobenzoic acid in man. *Eur J Clin Pharmacol.* 1976;10:283-7.
23. Du Souich P, Erill S. Metabolism of procainamide and p-aminobenzoic acid in patients with chronic liver disease. *Clin Pharmacol Ther.* 1977;22:588-95.
24. Du Souich P, Erill S. Metabolism of procainamide in patients with chronic heart failure, chronic respiratory failure and chronic renal failure. *Eur J Clin Pharmacol.* 1978;14:21-7.
25. Kobusch AB, Erill S, du Souich P. Relationship between changes in seromuroid concentrations and the rate of oxidation or acetylation of several substrates. *Drug Metab Dispos.* 1986;14:663-7.
26. Calvo, R, Carlos R, Erill S. Procaine hydrolysis defect in uremia does not appear to be due to carbamylation of plasma esterases. *Eur J Clin Pharmacol.* 1983;24:533-5.
27. Erill S. Drugs for the third world. *Science.* 1998;279(5350):462.
28. Erill S, editor. *Clinical Pharmacology through the Pen of Louis Lasagna. Pharmacotherapy Revisited: An Esteve Foundation Series. Vol. 1.* Barcelona: Prous Science, 1997.
29. Bosch F, Erill S, editors. *From Clinical Research to Clinical Pharmacology. Pharmacotherapy Revisited: An Esteve Foundation Series. Vol. 7.* Barcelona: Prous Science, 2006.
30. Wright P. Sir Gordon Wolstenholme [Obituari]. *Lancet.* 2004;364(9431):324.
31. Morales P, Bosch F. Empremta d'una tradició farmacèutica de segles en la Fundació Dr. Antoni Esteve. Gimbernat [Barcelona]. 2020;72:31-48.
32. Fundació Dr. Antoni Esteve. Barcelona, 2020. Consultable at: <http://www.esteve.org>. Accessed March 3, 2020.
33. Erill S, Bosch F. Fundació Dr. Antoni Esteve (Antoni Esteve i Subirana, 1902-1979), vint anys després de la seva mort. *Annals de Medicina.* 1999;82:293-4.
34. Erill S. Presentación. A: Periodismo científico. Un simposio internacional. *Monografías Dr. Antonio Esteve, núm. 12.* Barcelona: Ediciones Doyma, 1991, p. 9.
35. Erill S. The fluidity of truth. *Lancet.* 2001;357:1896.
36. Erill S. Wrong? And so what! *Lancet.* 2001;358:1740.
37. Erill S. Is it clinically significant? *Lancet.* 2002;359:1708.
38. Erill S. Let's waste our time! *Lancet.* 2003;362:1864.
39. *Els medicaments i jo.* Barcelona: Fundació Dr. Antoni Esteve, 2014.
40. Erill S. *La ciència oculta.* Barcelona: Fundació Dr. Antoni Esteve, 2017.

41. Vocabulari mèdic. Barcelona: Acadèmia de Ciències Mèdiques de Catalunya i de Balears, 1974.
42. Bosch F, Baños JE, Cobos A. Diccionari de recerca clínica de medicaments. Barcelona: TERMCAT i Fundació Dr. Antoni Esteve, 2014.