HISTORY AND HUMANITIES IN DERMATOLOGY

The Beginnings of Dermatopathology and Dermatologic Microbiology in Spain

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Abstract  Crisóstomo Martínez from Valencia was a pioneering microscopist in 17th-century Europe. The first microscopic representations of skin in Spain appeared in an 18th-century work by Martín Martínez. Microbiology and histopathology progressed considerably in the late 19th century thanks to anatomists like Maestre de San Juan and surgeons like Federico Rubio Gali. The first Spanish pathologist to specialize in dermatology was Antonio Mendoza, a colleague of José Eugenio de Olavide at the Hospital San Juan de Dios in Madrid. Claudio Sala and Juan de Azúa also made significant contributions, including the description of pseudoepithelioma.

Several disciples of Santiago Ramón y Cajal and Jorge Francisco Tello, such as Lorenzo Ruiz de Arcaute and Guillermo de la Rosa King, consolidated the dermatology laboratory, but the Civil War sent many into exile or deprived them of their professional status.

Juan Rubió in Barcelona and Julio Rodríguez Puchol in Madrid were the immediate predeces-sors of today’s dermatopathologists.

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Los comienzos de la Dermatopatología y de la Microbiología dermatológica en España

Resumen  El valenciano Crisóstomo Martínez fue un microscopista pionero en Europa en el siglo xvii. Las primeras representaciones microscópicas cutáneas en España aparecen en una obra del siglo xviii de Martín Martínez.

La microbiología y la histopatología progresaron mucho a finales del siglo xix gracias a anatomistas, como Maestre de San Juan, y cirujanos, como Federico Rubio Gali.

El primer dermatopatólogo español fue Antonio Mendoza, colaborador de José Eugenio de Olavide en el Hospital de San Juan de Dios de Madrid. Claudio Sala hizo importantes aportaciones con Azúa, como la descripción de los pseudoepiteliomas.

Algunos discípulos de Santiago Ramón y Cajal y Jorge Francisco Tello, como Lorenzo Ruiz de Arcaute y Guillermo de la Rosa King, consolidaron el laboratorio dermatológico. La Guerra Civil española llevó a muchos al exilio o a la depuración.

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Introduction

Medicine is multidisciplinary by nature, but the characteristics of each discipline’s store of knowledge and its peculiar requirements mean that some branches have more in common than others. Dermatology is especially dependent on microbiology and above all on pathology, to the extent that we remain unable to conceive of good clinical practice in our specialty without their support. This is the case even as our need for knowledge of genetics and immunology becomes as great or greater. By the second half of the 19th century, both microbiology and pathology had already taken their familiar forms. Their practices developed somewhat later than those of dermatology itself, whose origins can be traced to the beginning of the same century.

Thus, the 3 specialties emerged and developed in Spain almost simultaneously. All were in evidence in the second half of the 19th century and were well established by the first third of the 20th. In fact, dermatology—through the pioneering laboratory of Hospital de San Juan de Dios in Madrid—provided essential support for the advancement of histopathology and microbiology.

This article reviews the fundamental principles, history, and interrelations that brought pathology, microbiology, and dermatology together in Spain, covering the early period of emergence and consolidation in the second half of the 19th century and their coming of age in the first half of the 20th. As the story has been little studied and microbiologists, pathologists, and dermatologists are not fully aware of it, this record represents a modest effort to pay homage to the historical contribution of the laboratory technicians whose work provided the background for clinical practice.

Sources of Information on Dermatology and the Specialty’s Relation to Microbiology and Pathology

Very few studies have explored the relations among the 3 disciplines under consideration here. Ten years ago, Félix Contreras Rubio1 published a brief overview of the recent history of dermatopathology in Spain, and Julio Bassas-Vila2 has also provided general reflections on the subject.

A key secondary source of information about the early period of Spanish pathology is the doctoral thesis of Roberto Marco Cuéllar,3 written under the supervision of Professor José María López Piñero in Valencia and completed in 1966. This excellent thesis was rigorous and almost encyclopedic in its scope, as it delved into the emergence and early development of pathology before Ramón y Cajal. Surprisingly, it has never been published, although Marco Cuéllar took some material from his thesis for a chapter on histology and cytology in the fifth volume of the monumental history of medicine edited by Pedro Lain Enralgo (Historia Universal de la Medicina). After receiving degrees in both chemistry and medicine, Marco Cuéllar went on to earn his PhD in medicine. He then began a career in biochemistry and in 1984 became full professor of that subject at the Universidad Autónoma de Madrid. His career pathway perhaps explains the limited public dissemination of his thesis on the history of medicine. Marco Cuéllar died on June 27, 2008.4

The history of microbiology in Spain has been thoroughly studied by María José Báguena Cervellera,5 whose thesis on that subject was also supervised by López Piñero. This thesis likewise remains unpublished, even though it is rigorous and the amount of information it holds makes it worthy of wider circulation and publication.

Finally, the present author’s doctoral thesis on the history of dermatology,6 completed in 1996 under the supervision of Professor Antonio García Pérez, covered the origins of the school of dermatologic theory and practice in Madrid, the first to appear in this field in Spain. This thesis was based on a considerable number of primary sources and original documents.

The Early Years of Microscopy: Crisóstomo Martinez, the First of the Spanish Microscopists

Early microscopes are said to have been mainly used to entertain rather than to serve medical purposes. Microscopes were available as early as the first decades of the 17th century, but it was the curiosity of a Dutch merchant, Antonie van Leeuwenhoek, that led him to polish lenses and design instruments capable of magnification ×240, thus opening up a view of a previously unimagined world and making real progress possible. The first to see ciliates and other protozoa in water, van Leeuwenhoek called them animalcules and gave a full account of his observations in letters to the Royal Society of London; he also saw sperm cells, although he did not form a clear notion of their significance, and he may have seen red blood cells and bacteria. Nearly 2 centuries would have to pass, however, before this knowledge would be applied in medicine.

Robert Hooke, who was nearly a contemporary of van Leeuwenhoek, authored an interesting treatise titled Micrographia, published in 1665. Another noteworthy 17th-century user of microscopes was the Italian Marcelo Malpighi. His name is familiar to us today because of an eponymous term: the Malpighian layer of the skin, referring to the nucleated basal, spinous, and granular strata of the epidermis, excluding the stratum corneum.

Among the first Spaniards to use the new instrument was Crisóstomo Martínez (1638–1694), who was a member of the first generation of microscopists that included van Leeuwenhoek and Hooke. Martínez left a beautiful collection of engravings showing the structure of bone. In a still
life decorating the edge of one of the anatomical illustrations, there is a single-lens microscope (Fig. 1). This detail was used on the front cover of a monograph on the history of microscopic anatomy in 17th- and 18th-century Spain by María Luz Terrada Ferrandis.

Earliest Microscopic Images of the Skin in the Spanish Medical Literature

Martín Martínez, a celebrated Spanish physician at the end of the 17th century and beginning of the 18th century, was responsible for what were probably the first illustrations of the skin as seen under a microscope to be published in Spain. The 2 small illustrations appeared in a 1728 human anatomy book, inserted into the upper corners of a plate. The one depicting a reticulated pattern in the upper right corner (Fig. 2) was described thus by Martínez as showing “a portion of the skin with its epidermis.” The other drawing (Fig. 3), which was also given the number 3 in the source text, was said to represent “the manufacture of the skin, as revealed under the microscope: A. Cutaneous glands. B. Nerve papillae. C. Pores. D. Hairs. E. Subcutaneous vessels.” Exaggerated bumps appear on the surface of the skin and the hairs have very unrealistic branches; clearly this drawing reflects either the microscopist’s misinterpretation or the engraver’s artistic license.

Over the course of the 19th century, particularly between 1825 and 1875, the microscopic structures of the skin gradually became familiar. By the last quarter of the century, Spanish dermatology texts were being published with plates depicting cutaneous structures in detail. One of the earliest was Olavide’s monumental general dermatology textbook published in 1871. Several plates show histologic structures of the skin and adnexa. Interesting illustrations of histologic sections (Fig. 4) can also be found in a somewhat forgotten and less costly alternative to Olavide’s much larger and more attractive work. This was the clinical manual (del libro) on dermatology by Jerónimo Pérez Ortiz, published in 1886. Neither author seems to have prepared the histologic sections that illustrate their work, however. Rather, they seem to have reproduced illustrations and borrowed information from books already in print elsewhere in Europe.

Improvements in Microscopes and Staining Methods in the 19th Century

The methods used in microscopy advanced relatively little in the 18th century. Instruments were simple single-lens devices that could reveal little more than van Leeuwenhoek had managed to see. Furthermore, both these simple devices and the early compound microscopes distorted shapes and colors. After 1820 these problems began to disappear with the arrival of new lenses manufactured and polished mainly in England. Pioneers in the development of compound microscopes free of optical distortions were Carl Zeiss, in Germany, and Camille Sebastien Nachet, in France.
The instruments collected by Professor Eliseo Carrascal at the University of Salamanca admirably trace the evolution of microscopes and the variations in their design. Several Internet sites display photographs of microscopes from this period and explain their characteristics.

Marco Cuéllar mentions a book by Antonio Mendoza y Rueda, published in Barcelona in 1850. Though the author’s title referred to clinical studies in surgery, the second part of the volume had a large section on the microscope and its most important practical applications. Lesson 19 covered both simple and compound microscopes and their main accessories, such as diaphragms, condensers, the camera obscura and the camera lucida (or camera clara), prisms, etc. Mendoza y Rueda also discussed how objects are prepared for viewing—using the methods of Purkinje, Hannover, Jacobson and Raspail—as well as the double-bladed knife developed by Valentin for cutting thin sections.

Another key advance was the move away from reflected light toward better systems of specimen illumination, which compound microscopes required. The middle quarters of the 19th century witnessed great improvements in microtomes, illumination, and staining methods.

Specimen dissection was the subject of a book by José María Gómez Alamá (Arte de disecar). Its second edition (1872) included important references to different types of single-lens and compound microscopes. Included were solar microscopes and models incorporating early arc lamps. He also discussed the various types of micrometers (some with threaded screws, others with scales etched into glass disks), and set out guidelines for achieving adequate illumination of objects by reflection or transmission. Gómez Alamá named 2 conditions to meet when preparing tissue samples: the section must be extremely thin and the surfaces must be perfectly flat. To help readers achieve both requirements,
he gave advice on managing scalpels, fine saws, and polishing stones for bones or minerals. Marco Cuéllar\textsuperscript{7} reports that he mentioned an early version of a microtome by Strauss-Dürchen (sic.), a reference to Strauss-Dürckheim. The book contains illustrations of various instruments used at the time (Fig. 5).

This same period saw the introduction of a well-known staining technique for classifying bacteria into 2 broad groups. The system is the same one we use today and was proposed in 1884 by Hans Christian Gram of Denmark.\textsuperscript{10} Early methods for working with microscopes grew out of a great deal of experimentation and required skilled craftsmanship. One of the most interesting accounts of the process of staining samples for microscopy at the end of the 19th century was written in the field of dermatology, specifically the doctoral thesis on \textit{Achorion schoenleinii} and tinea favosa, by José Olavide Malo,\textsuperscript{11} the son of José Eugenio de Olavide Landazába. The thesis, which was published in 1888, gave a detailed description of how fungal samples were prepared. First the material was placed in an antiseptic solution (mercury chloride at a concentration of 1 part per 1000) for 2 minutes. It was then inserted into a tube with gelatin, cooled to 40 °C and cooled further under running water until the gel had solidified, and finally incubated at a temperature of 27 °C to 28 °C. Fungal colonies appeared in 6 to 8 days and could then be studied under a microscope. Olavide Malo proposed 5 steps, and they are quoted here for the historical interest of the description:

"1st, the organic matter is softened in an alkaline solution, preferably one containing potassium; 2nd, oils are removed by treating the fungus with alcohol followed by sulfuric ether or chloroform or any other solvent of oils; 3rd, portions of the vegetable material is stained: one should choose potassium, to give a blue color, or eosin in water, or Bismarck brown...; 4th, the vegetable material is then treated with a very strong solution (equal parts) of potassium acetate and distilled water in order to dissolve the excess color taken up by the bulk of the primitive stem so that the tissue is more transparent; and 5th, the sample is finally fixed on a slide: instead of Canada balsam, use a thick gum in solution, adding a few drops of phenic acid to prevent the fungi from escaping into the air."

Olavide Malo went on to explain how he undertook mycologic studies by growing the samples to increase the volume and embedding the material in paraffin (as well as in gelatin and in soap, although these media were judged inferior to paraffin) for later slicing with the freezing microtome introduced by Thomas Taylor or the rocking microtome manufactured by the Cambridge Instrument Company. Of the second microtome, the author says, "It is very appropriate for this type of work, providing an excellent series of slices with paraffin edges that line up squarely as they leave the microtome on a conveyor belt some 50 or 60 cm long."

A year before Olavide Malo presented his thesis to the tribunal, Julio Magraner Marinas\textsuperscript{8} had already written the following summary of a quarter of a century of work in this field:

"Work done with microscopes over the past 25 years has revealed that animals contain within themselves numerous colonies of living organisms; although many of these organisms are harmless, some are closely joined to the existence and production of various diseases. It was a question of experimenting, and now our experiments have answered in the affirmative."

Within a few years, he would be proven right.

**Microscopy Arrives in 19th-Century Spain by Way of Paris**

Most of our knowledge of histology and pathology dates from the period between 1825 and 1848. The main contributors were German scientists like Henle, Purkinje, Müller, Schwann, and Schleiden. Soon after this period, the circle that formed around Rudolf Virchow would play a key role. However, modern microscopic methods traveled to 19th-century Spain by way of Paris. Interestingly, a Venezuelan microbiologist—Eloy Carlos Ordóñez Sordo, whom most sources refer to simply as Ordóñez—was closely linked to the development of techniques in Spain. Ordóñez Sordo was born in 1822 in Giron, a village in the province of Pamplona in Nueva Granada, one of the 3 republics of the old state of Gran Colombia. His parents were from Maracaibo, Venezuela, and he studied in Santa Fe de Bogotá. After graduation, he accompanied Archbishop Mosquera on a journey from Colombia to New York, where he stayed for 2 years. On the archbishop’s death, Ordóñez Sordo settled in Paris and...
devoted himself to the study of microscopy, probably from 1851 onward. He died on May 19, 1868, at the age of 46 years.

In discussing dermatopathology, Marco Cuéllar cites the 1858 French publications of Ordóñez Sordo: a report describing a pigmented tumor—probably a melanoma—in the Bulletin de la Société d'Anatomie; a report to the Society of Biologists in France on an indurated chancre on the foreskin which was reviewed in the Spanish bulletins El Siglo Médico and El Compilador Médico; and another 1863 report on hair muscles written for the same biology association.

Ordóñez Sordo proposed a system for classifying tissues into 16 groups, which Aureliano Maestre de San Juan included in his book on general anatomy. Marco Cuéllar lists them as fibrillar (cellular, laminar, or conjunctival), fibrous (transient, fibro-plastic), elastic, adipose, cartilaginous, osseous, animal muscular (striated muscle), organic muscular (smooth muscle), epithelial, hyaline or anhistic, pigmented (lamina fusca, choroid, skin), retinal, nervous, enamel (of teeth), ivory (also of teeth), and crystalline.

Two men who studied under Ordóñez Sordo—Aureliano Maestre de San Juan and Federico Rubio Galí—established schools of practice in the last quarter of the 19th century. The first was associated largely with university laboratories and was the result of Maestre de San Juan’s interest in the pure study of morphology and histology, in keeping with his training as an anatomist. The second reflected Rubio Galí’s more clinical inclinations. His work involved a less constrained style of extramural education and leaned more clearly in the direction of pathology.

Aureliano Maestre de San Juan

An eminent anatomist, Maestre de San Juan (Fig. 6) established a solid foundation for histology in Spain, according to the account of Marco Cuéllar. He largely renounced research that could lead to original contributions in order to carry out the more mundane task of building up a store of information. Thus, he saw himself more as a laboratory technician than a scholar, and he shared his knowledge with his contemporaries. Born in Granada on October 17, 1828, he took his degree in the first stage of medical studies (bachillerato) in the same city and then spent 3 years completing his medical education in Madrid, where he graduated on November 8, 1847, at the age of 19 years. He received his doctorate in Madrid in 1851 and returned to Granada in 1856 to work as a clinical professor in the university’s faculty of medicine. In 1860 he competed for a professorship in general anatomy in Granada and occupied that position until he returned to Madrid in 1873 to take up a full professorship in normal and pathologic histology. A laboratory accident caused chemical burns that cost him his sight in 1888, and he died in Alicante on June 1, 1890. Maestre de San Juan lived simply, spending most of his money on books and materials for his work with the microscope.

One of this anatomist’s most important contributions was to found the Histologic Society on February 22, 1874, in the company of Andrés del Busto, Miguel Colmeiro, Gabriel de la Puerta, and the Venezuelan Francisco José Delgado Jugo, among others. None of these men were engaged with the fields of dermatopathology or skin microbiology, probably because they felt no need to confine themselves to such specific areas at this time. The society they founded was short-lived—it disappeared after 3 years—but the section on histology of the Academy of Physicians and Surgeons of Madrid carried the project forward. The formation of the Histologic Society was thus an important step toward laying a solid foundation for microscopic research in Spain.

Marco Cuéllar reports that in 1879 Maestre de San Juan published a treatise on normal and pathologic histology that included a discussion of laboratory technique (Tratado elemental de Histología normal y patológica precedido de un resumen de técnica de laboratorio). A second, extensively revised edition published in 1885 dealt with the compound microscope in greater depth and gave a good discussion of the Natchet (Fig. 7) and Verick microscopes, the camera lucida, micrometers, polarization devices, goniometers, immersion lenses, correction, heated slides and other specimen holders, rotating components, mounts for dissection, prism inverters, the Abbe condenser, and the spectroscope. A section on chemicals, vehicles, and reagents covered harmless vehicles (water, physiologic serum, amniotic fluid), reagents (alcohol and acetic, chromic, picric and other acids), preserving agents (glycerin, turpentine), cements (bitumen of Judea, Zeigler’s bitumen), stains that impregnate tissues (silver nitrate, gold or palladium chloride, osmic
acid), and stains that act by inhibition (carmine, picricarminate, Ranvier purpurin, sulfate, and rosiniline acetate, fuchsin or aniline red, quinoline blue, hematoxylin, indigo carmine, eosin, and more). Also discussed were preserving and clearing agents such as glycerin, turpentine, Canada balsam, clove oil, and dammar resin.2

Although Maestre de San Juan initially hesitated to align himself with a particular approach, he finally opted to follow Rudolf Virchow’s German school of histology, while still conscious of the debt he owed his French training. He used, for example, a Ranvier microtome, which was little more than a screw and shaving razor. Methods for fixing samples were being introduced at this time. Initially, gum arabic was used. Freezing was also discussed, although it was felt to be difficult to find equipment that could achieve the desired result.

Federico Rubio Galí

Another key figure, was Rubio Galí (Fig. 8), a histologist and surgeon whose interest in the microscope dated from the time he spent working in Seville. There, he joined a group of surgeons who used histologic techniques themselves or took an interest in them. Others in this circle, Marco Cuéllar3 reports, were Adolfo Moreno Pozo, Juan Creus Manso, Santiago González Encinas, and José Calvo Martín.

Rubio Galí was born in Puerto de Santa María in 1827 and studied medicine in Cadiz, graduating in 1850 with high marks. He won a post at the Hospital Central de Sevilla that same year, but his political liberalism led to serious professional setbacks. At one point he had to give classes in fencing—a skill he excelled at—in order to make ends meet. His interest in histology began during a period of exile to France, where he became interested in Ordóñez Sordo, according to Marco Cuéllar.3 He returned to Seville for a time and later worked in Madrid.

In 1872 he authored a paper on an analysis of air in the hospital wards of Dr Ezequiel Martín de Pedro in the Hospital General de Madrid1; the analysis was accomplished in collaboration with José Eugenio de Olavide. They found various bacteria and described 3 types: bacterium punctum (which we would refer to as cocci today), bacterium catenula (chains of 2—i.e., diplococci—or 3 cocci), and bacterium baculum (bacilli). The publication even described how these bacteria moved.

Most of the histologic preparations for the autopsies Olavide later described in his anatomic atlas were done by Rubio Gali. Some of these preparations, even made it possible to supplement the color plates of the atlas with black and white illustrations of clinical lesions (Figs. 9 and 10).

Salvador Cardenal

Born in Valencia in 1852, Salvador Cardenal studied to be a surgeon in Barcelona, graduating in 1875. Cardenal’s report on histologic and clinical characteristics of lupus, epithelioma, and ulcerating tumors, which also compared their different treatments, won a competition organized by the Royal Academy of Medicine in Madrid. Marco Cuéllar3
notes that the report revealed Cardenal’s considerable understanding of histologic techniques and a wide range of stains and fixing agents. Cardenal recommended carminic acid with the addition of picric acid to stain epithelioma samples, for example. He also published a manual on surgical antisepsis, of which several editions were printed.

Cardenal’s work gave evidence of the many advances that led to enormous growth in knowledge in the field of microbiology in the last third of the 19th century, according to Báguena Cervellera. Relevant advances included improvements in the manufacture of microscopes (better objectives and apochromatic light-condensing lenses) and the use of aniline dyes to stain microorganisms.

Some Contributions of Spanish Microbiology to Epidemiology

The study of infectious diseases was an independently progressing field that furthered the development of microscopy, as presented by Báguena Cervellera in her thesis. Pablo Colvée, for example, demonstrated the means of contagion during an epidemic of trichinosis in the town of Villar del Arzobispo in 1877. Vicente Peset Cervera, who had studied both medicine and chemistry, published on the role of fermentation in physiology and pathology in 1878. His meticulous studies of the fermentation of foods in the digestive tract followed a line similar to Pasteur’s. From this work it was possible to infer the existence of microorganisms that promoted the digestive process, ultimately undermining the theory of spontaneous generation.

Báguena Cervellera also describes an 1898 textbook on basic microbiology for students of human and veterinary medicine by Luis del Río y Lara, professor of histology at the university in Saragossa. Del Río y Lara’s book was the first to present microbiology as a discipline separate from pathology. A considerable number of pages in this book were devoted to 3 diseases relevant to dermatology: actinomycosis, tuberculosis in its various forms, and leprosy. Cocci (staphylococci, streptococci, tetrad, and sarcinae) were mentioned in relation to phlegmon- and abscess-causing pyoderma. Del Río y Lara also studied lymphangitis, erysipelas (which he referred to as streptococcal dermatitis of Fehleisen) and carbuncles. Syphilis, trypanosomiasis (durina), and gonococcal infection were also given ample treatment. Del Río y Lara customarily used a glycerinated gel-forming broth that already contained agar-agar and resembled the media used in microbiology today.

José Eugenio de Olavide published a short paper on Vibrio cholerae in 1884, the same year Robert Koch described this bacterium. This publication apparently bore no relation to his practice of dermatology. He was working at the laboratory of Hospital San Juan de Dios, which belonged to the provincial government of Madrid (the Diputación). This hospital was a center of reference in the effort to control the
cholera epidemics raging in Spain at the end of the 19th century.

**Plant and Animal Parasitism**

Dermatology played an important role in helping the concept of contagion take root in medicine because lice infestation and scabies provided the paradigm for parasitic diseases in general and for disease transmission. It was reasoned that if lice and mites could pass from one individual to another and cause disease, even smaller parasites that were as yet unidentified could also do so.

José Eugenio de Olavide’s atlas of anatomy contained a magnificent illustration of the *Sarcoptes scabiei* mite and explained the transmission of scabies.

Báguena Cervellera also notes the gradual acceptance of the idea that plants—fungi to be precise—could sometimes cause disease after Agostino Bassi demonstrated, around 1830, that a fungus was responsible for muscardine in silk worms. Just such a fungal disease provides the starting point for the story in Alessandro Baricco’s recent successful novel, *Silk*.

The first studies of parasitic plants were done by botanists. Johann Schönlein, Jacob Henle, and Ernest Bazin were outstanding contributors to this branch of knowledge in the middle decades of the 19th century; other names associated with parasitic plant studies included Gruby, Richter, Audouin, Vogel, and Lebert. In the previously mentioned monograph on cholera by Olavide, it is interesting that he referred to the bacterial pathogen as a “microscopic plant.” The influence of botany on microbiology may surprise us today, but even now our language reflects the ties between these disciplines, as we continue to refer to microorganisms in general as germs.

**Historically Important Research Facilities**

Laboratories were—and continue to be—the places where microbiologists and dermatopathologists conduct their research. Therefore, it is essential to name the important research facilities as well as the relevant scientists. Báguena Cervellera described them in her thesis. One was the outstanding laboratory for the study of normal histology, pathology, and bacteriology founded in 1875 by Maestre de San Juan at the faculty of medicine in Madrid. Another important laboratory in the same city was the National Institute of Hygiene and Bacteriology, established in 1894. This facility would grow into the larger National Institute of Serotherapy, Vaccination and Bacteriology (also called the Alfonso XIII National Institute of Hygiene), which was created by Royal Decree on October 28, 1899. The laboratory at Madrid’s military hospital—where Rafael Ariza and José Alabern worked—must also be mentioned. That facility undertook both chemical and microscopic studies. Finally, the laboratory of Hospital de San Juan de Dios mentioned earlier will merit special attention in a separate section below.

The city of Barcelona created its own municipal laboratory in 1887. Also noteworthy in the same city were the Ferrán Institute (where Jaime Ferrán did his work) and the Institute of Biology (where Ramón Turró worked).

**Microscopy and Histochemistry: Microbiology, Pathology, and Clinical Biochemistry**

Given our current notion of microbiology, pathology, and clinical biochemistry as distinct disciplines, it seems striking to us today that the early microscopists worked simultaneously in all these branches of knowledge. Microbiology and pathology were thrown together for a simple reason: they used the same tool—the microscope—as well as similar chemicals for analysis and staining. The term microscopy (or the contemporary alternative micrography) originally encompassed both those disciplines and was widely used inclusively to refer to them at the end of the 19th century. The link to clinical biochemistry may seem more tenuous, but in fact this field was once called histochemistry, a term that has been recycled in recent decades with a completely new meaning. The connection was that the microscopy laboratory was also the place for performing chemical tests. Some contemporary dermatology textbooks referred to technicians in all these fields simply as laboratory men.

The end of the 19th century saw lines drawn between microscopy as practiced by pathologists on the one hand and microbiologists on the other. It was Luis del Río y Lara, mentioned earlier, who brought about this change.

In dermatology, however, the so-called laboratory men would continue to have broad areas of practice, working as pathologists, microbiologists, and mycologists while at the same time performing serology and other analyses.

**Microscopy, Microphotography, and Pathologists as Draftsmen**

The distinction between microscopy and microphotography (also termed photomicrography) should be underlined. The earliest photoengravings of histologic sections date from the beginning of the 20th century, and the first volume of the journal *Actas Dermofisiográficas* (1909–1910) contained several such illustrations. Microphotography was a bit of a luxury, however, and early researchers did not routinely use it. This meant that they were obliged to develop competence as draftsmen so they could accurately represent what they saw through their microscopes. Contreras Rubio noted that drawing remained a valued skill until very recently. The cultivation of this avocation—or even essential craft—meant that certain classical European dermatopathologists, such as Felix Pinkus and Achille Civatte, became fine draftsmen who left us curious caricatures and miniature works of art in their laboratory notebooks and manuscripts.

**The Olavides: Father and Son**

José Eugenio de Olavide became familiar with the microscope while still a student. As early as 1857, when he summarized the case of a patient from whom his supervisor, Manuel Soler, had removed a tumor, Olavide remarked that “the microscope revealed only globules of fat.” Mentioned earlier was Olavide and Federico Rubio Gali’s analysis of the air in the wards under Dr Martín de Pedro to see
if it contained potentially pathogenic microorganisms; that collaboration led to the 1872 paper by Rubio Gali.\textsuperscript{12}

On his own, Olavide studied fungi under the microscope, sometimes commenting on observations made at magnifications of $\times 350$ and $\times 700$. However, when it was necessary to prepare tissue and other pathologic samples for viewing through a microscope, Olavide relied on Rubio Gali’s expertise.

Olavide made it clear in his publications that he was convinced that scabies, filariasis, and tinea were caused by living microorganisms. He was also the most prominent promoter of the concept of plant and animal parasitism in Spanish dermatology at the time. One of his most celebrated experiments—carried out with Rubio Gali and Benito Hernando Espinosa—was successfully transmitting tinea from a patient to 3 animals: a mouse, a cat, and a dog. The mouse died, but the dog escaped, running through the precincts of the hospital—according to Olavide’s own account—until a member of the hospital’s staff, fearing he would himself be infected, turned the animal loose on the street, where it soon vanished. Olavide’s talk on his induction into the Royal National Academy of Medicine and several articles in a Spanish journal covering ophthalmology, venereology, dermatology, and urologic diseases (Revista Especial de Oftalmología, Sifiliografía, Dermatología y Afecciones Urinarias) also dealt with plant and animal parasitism. He argued that contagion was a fundamental concept of pathogenesis, naming 3 types: parasitic, miasmatic, and virulent. Scabies and mycoses provided paradigms for the first type, miasmatic contagion, as Olavide understood it, was related to fermentation. Finally, in virulent contagion, the infectious agent would be a fluid (of a purulent or serous type).

José Olavide Malo, José Eugenio’s son, was also a dermatologist and a founding member of the Spanish Society of Dermatology. Mentioned earlier was Olavide Malo’s doctoral thesis on Trichophyton schoenleinii—classified as Achorion schoenleinii at that time.

**Antonio Mendoza and the Laboratory at Hospital de San Juan de Dios in Madrid**

José Eugenio de Olavide was the driving force behind the establishment of the laboratory at Hospital de San Juan de Dios in its first location (Plaza de Antón Martín) and he served as its head, but the true star of this enterprise was one Antonio Mendoza (Fig. 11), who must not be confused with Antonio Mendoza y Rueda, professor of surgery at the University of Barcelona. Mendoza the microscopist (1848–1917) worked more in microbiology than dermatopathology, and he was particularly expert in methods for isolating and observing germs. It was Olavide who brought Mendoza from Cadiz to Hospital de San Juan de Dios, advancing much of the cost of Mendoza’s work out of his own pocket, though he was later reimbursed through funds from the provincial government of Madrid (the Diputación) through the accounts of the public charity hospital (Beneficencia Provincial).

Mendoza was a highly skilled microbiologist and laboratory technician. Some of his contemporaries—notably Rafael Ariza—considered him to have a weakness for comfort and luxury, but this tendency is easy to understand if we remember the underlying vulnerability of his economic situation.

![Figure 11](Image)

Figure 11 Caricature of Antonio Mendoza, microscopist at Hospital de San Juan de Dios in Madrid, published in a magazine of medical satire, El Doctor Sangredo. The egg Mendoza is hatching from is a reference to cytology, and bacteria (coci, rods, and spirilla) can be seen along the upper edge of the drawing.

What is certain is that Mendoza’s expertise yielded remarkable results in the laboratory. Some decades later, Salin de Aja\textsuperscript{10} recounted an anecdote, possibly with slight exaggeration: “When Dr Mendoza presided over the laboratory at Hospital de San Juan de Dios, encouraged by Dr Olavide’s progressive, research-oriented spirit, he made this suggestion: “What do you think if we put up a sign saying, ‘Discoveries made in this laboratory this week’?”\textsuperscript{12}”

This hospital laboratory had cutting edge equipment. In 1880, Maestre de San Juan even mentioned in passing that they had a device for projecting images of what they saw under the microscope:

“[For classroom instruction in our department we use various types of microscopes to examine fresh specimens, and we also have other fixed specimens in collections as well as atlases and line drawings for coloring. In some sessions we use Dr Le Bon’s device to project lantern slides. For 8 years we have been using this projector, which is similar to Molteni’s, and have added a microscope to the apparatus in a way that magnifies the slides without the preparations becoming damaged by heat. The pharmacy department (Professor Lieget) has the latest model, and there is another one
named as second coauthor on 6 publications, more often than any other microbiologist except Jaime Ferrán.

**Claudio Sala Pons**

Sala Pons merits a place of honor in the history of Spanish dermatopathology, even if only for his collaboration with Juan de Azúa in describing pseudoepithelioma (vegetative pyoderma). I have been unable to learn a great deal about his personal history, but he was a follower of Ramón y Cajal, working with him between 1892 and 1894. In the master’s recollections there is mention of their collaboration, which led to several titles by Sala Pons on the spinal cord of amphibians (Barcelona, 1890), the cerebral cortex of birds (1893), and his thesis on the glial cells of vertebrates. Ramón y Cajal reported that Sala Pons presented the thesis to a tribunal in Barcelona in 1894.

On October 8, 1911, the newspaper ABC announced a course taught by Sala Pons at the faculty of medicine in Madrid. The initial lecture dealt with physical, chemical and microscopy techniques with clinical applications, including the reagents and equipment required by a laboratory. The announcement can now be found on the Internet. The monograph on pseudoepithelioma coauthored with Juan de Azúa lists Sala Pons’s affiliations as the faculties of pharmacy and sciences; specifically he was full professor in charge of microbiology at the faculty of pharmacy. Another historical document that can be accessed on the Internet mentions Sala Pons’s application for the directorship of the Museum of Natural Sciences in Barcelona in February 1921; his candidacy was rejected on the grounds that he was more than 45 years old.

Sala Pons and de Azúa worked closely together; de Azúa described a complicated case of cutaneous necrobiosis in a young male patient at an international medical conference in Madrid in 1903, using slides prepared by Sala Pons. The case report was published the following year with 2 excellent illustrations of the capillaries of the skin, a venule, and an arteriole. For the same conference, these men prepared another presentation on the possible microbial origin of eczema. However, it is their joint work on pseudoepitheliomas (Fig. 13) that perhaps marks their main contribution to the literature, as it is one of the first—if not the very first—descriptions of cutaneous pseudomalignancy.

**Juan Sanchez Puente: Pharmacists as Microbiologists**

Sanchez Puente, an enigmatic microbiologist working in the early years of the 20th century, became known for a monograph on the human leprosy bacillus published in 1915. At that time he was identified as having a PhD in pharmacy and had a post as pharmacist in the public charity hospital (Beneficencia Provincial) of Madrid. He presented himself at the beginning of the book, however, as chief of the laboratory at Hospital de San Juan de Dios in the same city and called himself a follower of Dr Castro, in whose microbiology laboratory he began his study of the leprosy bacillus.

Although we have little information about Sánchez Puente, he merits mention in the present article because he belonged to that outstanding group of pharmacists and

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**Figure 12** Plaque commemorating an analysis of the waters at the Cabeiroá spa in Verín, in the province of Ourense, in 1905. Antonio Mendoza signed the analysis in his capacity as a member of the staff of the Instituto Alfonso XIII, directed by Santiago Ramon y Cajal.

at the histochemistry laboratory at Hospital de San Juan de Dios here in Madrid.”

Olavide also noted that Mendoza was commissioned by the authorities to travel abroad in 1884 to study *Vibrio cholerae* shortly after it was identified by Robert Koch.

In 1899 a central health facility—the National Institute of Serotherapy, Vaccination and Bacteriology, also commonly referred to as the Alfonso XIII Institute—was founded by merging the National Institute of Hygiene and Bacteriology with the Central Institute of Vaccination. Antonio Mendoza was probably associated with this new facility from the beginning or joined the staff soon after it was founded. At the health spa in Cabeiroá, in the province of Ourense, the visitor can find a plaque giving details of a chemical analysis of the waters, dated 1905. The plaque shows a report of an analysis signed that year by Mendoza in his capacity as member of the staff of the national institute in Madrid (Fig. 12).

Finally, the historical sources that Bâguena Cervellera analyzed in her doctoral thesis revealed that Mendoza was
biologists who have been working in our hospital laboratories for a century now, even though we are often not aware that they initial trained in those disciplines.

**Pathology and Microbiology in Catalan Dermatology: Juan Giné Partagás and José Viñeta Bellaserra**

Juan Giné Partagás (Fig. 14) was a prominent figure at the start of Spanish dermatology, working in the field nearly as early as Olavide. His main accomplishment in microscopy was the translation of a 19th-century classic, Rudolf Virchow's great work on cellular pathology. Marco Cuéllar notes that Dr Bartolomeu Robert also worked on the translation, which was published by the journal *El Pabellón Médico*. In 1871 Giné Partagás was named professor of surgery at the faculty of medicine in Barcelona, succeeding Mendoza y Rueda. In the first stage of his professorship his interest centered on normal histology. His work in clinical histology came later. Marco Cuéllar notes that his interest in psychiatry toward the end of his life distanced Giné Partagás from histology. Several beautiful engravings illustrating the histologic structure of the skin appeared at the end of his book on surgical dermatology, which also contained clinical photographs.

Another Barcelona dermatologist, José Viñeta Bellaserra, was born in Havana in 1857. While an undergraduate, he studied with Giné Partagás but later worked with Olavide on his doctorate, which could only be earned in Madrid at that time. Viñeta Bellaserra continued his studies in Paris (Hôpital Saint-Louis), returning to Barcelona to work in 1882. That same year he published a study on cutaneous diphtheria in the journal *Revista de Ciencias Médicas*, and in 1883 there was a paper describing 5 cases of cutaneous lymphadenia, or Alibert mycosis fungoides. Each was accompanied by histopathologic analysis. Four of the cases were from the time he spent in Paris and the fifth was from Barcelona.

**Santiago Ramón y Cajal and Pío del Río Hortega**

It would be unpardonable to leave the father of Spanish histology out of this account, although it is true that Ramón y Cajal’s own contributions to the study of the skin, or dermatopathology, were scarce or nil. He focused his attention so specifically on nerve tissues—about which he made so many magnificent discoveries—that he practically ignored pathology and histology unrelated to the nervous system. However, some of his followers eventually contributed significantly to Spanish dermatopathology, so we can say that he did influence this discipline, but more through his creation.
of a school of practice than through direct contributions. His new staining methods were influential to a certain degree and were applied to skin samples.

Another figure to mention is Pío del Río Hortega. Interestingly, he appeared in 1909 as a founding member of the Spanish Society of Dermatology (later, the Academy). His residence was in Valladolid, and he was therefore listed as a supernumerary member (corresponsal nacional), a category reserved for those who did not live in the capital. Although there are no signs that del Río Hortega participated actively in the sessions of the Society or that he ever published in *Actas Dermo-Sifiliográficas*, his name appeared regularly on the annual roster of members.

**Dermatologists, Pathologists, and Microbiologists of the 1920s and 1930s**

The 1920s and 1930s were a period of excellence in the history of Spanish science. Authors like Nicolás Calvín, Guillermo de la Rosa King, and Lorenzo Ruiz de Arcaute kept alive the ties between dermatology and the laboratory bench during this time. That all three were serologists reflected the significance of these techniques in venereology after Wasserman's discoveries at the turn of the century. Both de la Rosa and Ruiz de Arcaute were followers of Jorge Francisco Tello, although Fernández de la Portilla described Ruiz de Arcaute as a direct disciple of Ramón y Cajal.

De la Rosa was chief of the pathology department at Hospital de la Princesa of Madrid, and he also worked at the venereal disease clinic of Juan de Azúa (Dispensario Azúa). An obituary in *Actas Dermo-Sifiliográficas* in 1944 noted that he had studied in New York, thus forging a trail that would be taken by the long and brilliant list of professionals who have since traveled across the Atlantic to complete their training. When Tello won the post of professor of histology and pathology at the faculty of medicine in 1926, Ruiz de Arcaute took up Tello's post at the Hospital Clínico de San Carlos. He was also connected with the Alfonso XIII Institute, according to de la Portilla. Both men worked with Martínez Anido in a clinic to treat venereal diseases in Madrid, on Calle de Sandoval, where the offices of the Spanish Academy of Dermatology and Venereology (AEDV) were located for several decades. De la Portilla was director of the clinic and Ruiz de Arcaute headed the laboratory. They taught several courses on syphilis, as we know from announcements in dermatology journals of the 1930s. In a 1919 issue of *Actas Dermo-Sifiliográficas*, Ruiz de Arcaute published an article with interesting additional information on pathologic aspects of a case report by Enrique Álvarez Salinas de Aja that had appeared earlier in the same journal. The subject was sclerosis and erythema affecting the fingers. Ruiz de Arcaute died in 1936 when Franco’s forces bombed Madrid during the Spanish Civil War. Three men, who died too soon, were part of a promising generation of laboratory dermatologists.

Another small group of dermatologists carried out their own microbiologic and pathology studies. One was Vicente Gimeno, assistant professor of dermatology with Juan de Azúa at the medical faculty in Madrid. In the early years of *Actas Dermo-Sifiliográficas*, he authored several papers describing his own dermatopathologic research. In a paper on multiple subcutaneous hydatid cysts, he set out to discuss “the first slides we prepared for observation under the microscope as well as the photographs taken in the general pathology laboratory of the faculty of medicine.” And in fact the text is accompanied by more than 36 interesting photoengravings. Contemporary accounts also describe José Gay Prieto preparing his own material for histology at least occasionally.

José Sánchez-Covisa and Julio Bejarano, who carried on the work of Juan de Azúa, presented an interesting study (in French) in Strasbourg in 1923. They had stained skin samples with the same silver nitrate method Ramón y Cajal and his followers had put to such good use for the study of nerves. They did not clarify whether they or their associates at Hospital de San Juan de Dios prepared the samples. Sánchez-Covisa had not yet acceded to the professorship in dermatology he would earn later and through which he would create a strong laboratory under the direction of Manuel Hombria Íñiguez. Stains based on a variety of silver salts must still have seemed novel and attractive in the 1940s. In 1943 Xavier Vilanova and Juan Rubió Roig published a modification of del Río Hortega’s method for staining epithelial fibrils.

**The Civil War: Purges and the Case of Manuel Hombria Íñiguez**

The case of Hombria Íñiguez offers an example of how lives were tragically disrupted by the Spanish Civil War, as it affected the population in general and dermatology in particular. Hombria Íñiguez’s brother Antonio—also a dermatologist—was executed by Franco’s troops when they took Cordoba in 1936, and as Hombria Íñiguez himself was not allowed to work in the public health system or in education, the years following the war were difficult. On December 19, 1940, at the College of Physicians in Madrid, he was declared unfit for posts that required public trust and was not rehabilitated politically until February 8, 1946. His death in 1953 was noted in *Actas Dermo-Sifiliográficas*. A large number of young physicians who trained in Madrid in the 1930s suffered the same fate and professional ostracism as Hombria Íñiguez. Among those most grievously affected were those who had studied under José Sánchez-Covisa—men like Servilliano Pineda, Covisa’s assistant for dermatology and photomicroscopy starting in 1932; Luis Vallejo Valdejo, assistant instructor of serology in the dermatology laboratory; and Emilio Enterría Gainza.

**Two Women in the History of Laboratory Dermatology in Spain**

Two women who worked in dermatology in Madrid and Barcelona in the 1930s were true pioneers in a field that was otherwise the exclusive province of men at the time. One of them, María de Castro Cantalapiedra, was named in one source as assistant professor for practical sessions under Sánchez-Covisa; however, she was later named in purges and no further information about her has come to light. The second woman, who worked in Barcelona, was
acknowledged as “Dr. J. Salvaus,” the supplier of the
anatomic and bacteriologic studies for a 1935 report in Actas
Dermo-Sifiliográficas on a case of pseudopelade of Brocq,
authored by Xavier Vilanova. 18

The Last of the Old Generation: Julio
Rodríguez Puchol and Juan Rubió Roig

The immediate predecessors of today’s dermatopathologists
are 2 outstanding figures: Julio Rodríguez Puchol in Madrid
and Juan Rubió Roig in Barcelona. Contreras Rubio11 men-
tioned them with respect. Rodríguez Puchol was a follower
of Tello and later worked with Ramón Martínez in the Hos-
pital del Rey.12 Pérez Peña13 mentions Rodríguez Puchol in
his book on physicians who were exiled or purged from the
medical faculty in Madrid, although evidence to confirm the
report is lacking. According to the author, Rodríguez Puchol
was born in Valladolid on April 23, 1912, studied medicine
in Madrid in the academic years of 1928–1929 and 1934–1935.
His grades were good and he was a student intern in pathol-
yogy. He graduated with a medical degree on March 23, 1942,
receiving his diploma in September 1943 and his PhD in 1960,
with a thesis on the histopathology of cutaneous angiitis
completed under the guidance of Fernando de Castro. He
completed specialist training in histopathology and cli-
nic biochemistry in Valladolid in 1965. As early as 1945,
Rodríguez Puchol 10 authored a publication in which his affil-
iation was given as head of the laboratory in the service
of Enrique Álvarez Sainz de Aja at Hospital de San Juan
de Dios. In that same academic year of 1945–1946, he was
listed as a member of the AEDV residing in Madrid (number
7, Calle de Campomanes). Gay Prieto designated him pro-
fessor of histopathology in the professional studies program
in dermatology under his direction at the university. With
Contreras Dueñas he served as assistant secretary of the
Sixth International Conference of Leprology held in Madrid
in 1953 and was then named professor of histopathology in
courses on leprosy given at the sanatorium in Fontitites,
Alicante, under the direction of Gay Prieto and Contreras
Dueñas.

Félix Contreras Rubio described Rodríguez Puchol as fol-
 lows in the inaugural talk at the Twenty-Second Confer-
ence of the Spanish Society of Pathology (SEAP) in Palma de
Mallorca in 2005: “He was a very well rounded general
pathologist with specialist knowledge of infectious diseases,
endocrinology, cardiology, cytolgy, and of course derma-
tology. He served on the Board of Directors of the Spanish
Academy of Dermatology for years and was founder and first
treasurer of our own Spanish Society of Pathology. Intelli-
gent, hard-working, cultivated, pleasant, and an excellent
teacher, he mentored many aspiring pathologists in those
early 1960s.” Rodríguez Puchol served as secretary of the
AEDV in the 1960s.

Juan Rubió Roig was another great name in Spanish der-
matopathology in the years after the Civil War. According
to Xavier Sierra Valenti, who kindly furnished me with a
few personal details, Rubió Roig was born on December 16,
1917, and died on January 21, 2003. His father, Joan Rubió
i Bellver, was an important Modernista architect who num-
bered among the successors of Gaudi. Rubió Roig finished his
undergraduate medical studies in 1934. He began working as
a teaching assistant at the University of Barcelona in 1965.

Contreras Rubio also provided a vivid portrait of Rubió
Roig in his opening talk at the SEAP conference: “Joan Rubió
was not much interested in presentations, publications, con-
ferences, or public acts of any type. He nonetheless played
a significant role in the international courses on surgical
pathology organized by Lorenzo Galindo in Barcelona. He
was a wonderful person, considerate and accomplished.
His many talents included an artistic inclination that he
expressed through painting. He was also inventive and
designed his own tools, such as a small microtome for
surgical biopsies. Another device was an apparatus that
automatically embedded samples in paraffin. Manufactured
by Myr, S. L. in Barcelona, this processor was the first to be
used in Spain when paraffin embedding was just becoming a
part of laboratories’ routine practice. In that unforgettable
laboratory at the department of dermatology in Barcelona,
many generations of dermatologists were taught as well as
all the pathologists who chose to spend shorter or longer
periods learning from him.”

Rubió Roig’s career was spent largely in the shadow of
Xavier Vilanova, whom he accompanied to posts at the
faculties in Valladolid, Valencia, and Barcelona. In some
of the papers he authored alone, his credentials were
given as departmental histopathologist. In Valencia, he
worked alongside José Esteller for a time. Rubió Roig’s name
first appeared on the roster of the AEDV in Volume 36
(1944–1945), when he was said to reside at number 190 on
Via Layetana in Barcelona.

From the Age of Pioneers to the Present

At the beginning of the 20th century, clinical biochemistry—
especially serology—and microbiology began to take paths
that led them to diverge somewhat from dermatology. The
ties between mycology and dermatology, on the other hand,
remained close. Dermatologists played notable roles in this
field in the 1930s and 1940s. Important were Eduardo de
Gregorio in Saragossa in the 1930s and 1940s, and Manuel
Pereiro Cuesta and Manuel Pereiro Migüens (father and son)
in Santiago de Compostela.

Names in the recent history of dermatopathology are
much more familiar to us than those mentioned earlier in
this article. Some, like Abelardo Moreno, an outstanding
pathologist, and Adolfo Aliaga, a superb dermatologist, are
no longer with us. They, along with their generation of men-
tors in America and other European countries, are the ones
who trained the young, rising group of dermatopathologists
who work beside us in our laboratories today.

Ethical Disclosures

Protection of human and animal subjects. The author
states that no experiments were performed on humans or
animals for this investigation.

Confidentiality of data. The author declares that he
followed the protocols of his hospital concerning the
publication of patient data, and that all the patients
The author declares that he has no conflicts of interest.

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