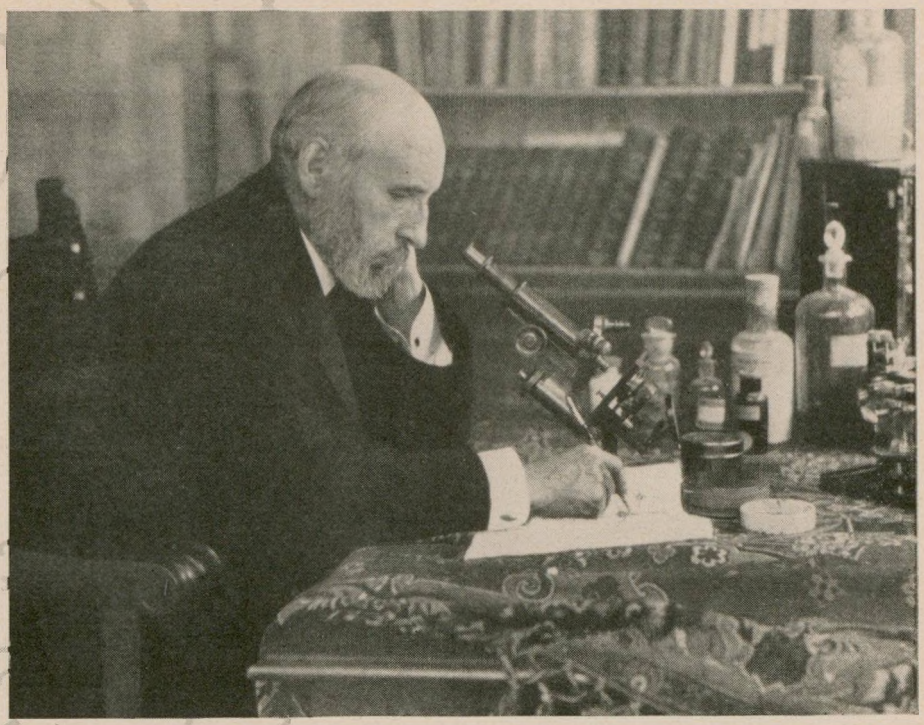

GIANT ANATOMIST

MD NEUROLOGY

▪ If anyone in the Spanish village of Ayerbe had been asked a hundred years ago what they expected the future of young Santiago Ramón y Cajal would be, the answer would in most cases have been the gallows.

The eldest son of a physician, Santiago was born on May 1, 1852. By the time he was eight he was leader of a gang of boys who pelted people with stones, raided orchards, pilfered indiscriminately, played practical (and often painful) jokes. When Santiago spent three days in jail for demolishing a neighbor's gate the villagers were convinced that the boy would come to an unsavory end.

At the College of the Aesculapian Fathers in Jaca, Santiago rebelled against learning Latin by rote, was flogged and locked up on prison fare. He was discharged, thin and sullen, placed in the Institute at Huesca, where instead of Latin he was taught mathematics and science, and instead of studying he spent most of his time on a secret course of physical training. The school report was as bad as expected and Santiago was given a course of study, under the stern direction of his father, that he would have to complete during the summer holidays. In the nearby attic of a pastrycook, where he went to pilfer pies, he discovered piles of old books; he thus came across *Robinson Crusoe* and other romances which were to play an important part in his formation. When the time for examinations came, he failed utterly, was taken from the school by his father and apprenticed to a barber.

In between cutting hair and shaving, Santiago continued his brigandage, defiant and miserable, scorned by honest folk and ostracized by the children of respectable families. In despair, his father apprenticed him to a shoemaker, a craft which he enjoyed.

When the boy was 16, his father began teaching him anatomy, finally admitted his remarkable talent for quick sketching which he had earlier tried to

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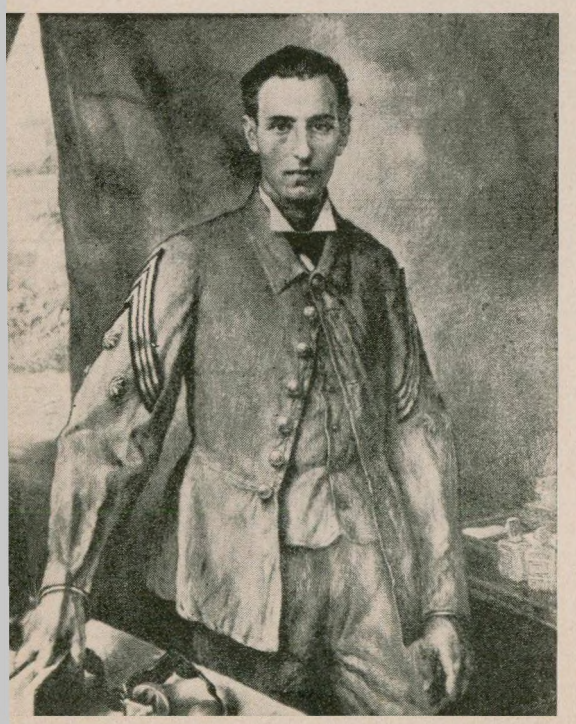
Doña Antonia and Don Justo, parents of Dr. Ramón y Cajal, photographed in 1907, after their son won a Nobel Prize.

Portrait of Ramón y Cajal, about 22 years old, when he was a medical officer in Cuba.



suppress. Santiago gave up his wayward ways, settled down to medical studies at the university of Saragossa where his father held a post as instructor in anatomy. The boy's anatomic sketches were so accurate that there was even talk of publishing them in an atlas.

In the summer of 1873, Santiago had reached his majority and obtained his licentiate in medicine. Spain was then again in political turmoil, the short-lived republic being faced with another Carlist war. Compulsory military service was decreed for all able-bodied men; Santiago was given the rank of lieutenant, appointed second medical aide in an infantry regiment that saw no fighting. After eight months he was sent in an expeditionary force to Cuba, then undergoing one of its periodic revolts against Spain.

He was assigned to direct one of the most isolated infirmaries on the island, at Vista Hermosa, in jungle territory and a region devastated by war. Wrote he later: "Those who have sung the praise of the tropics have overlooked one single small detail: that enchanting paradise is simply uninhabitable for a European."

About 200 patients in the infirmary were down with either malaria or dysentery; Ramón y Cajal slept near them separated only by a board partition. He fixed himself up a tiny photographic laboratory using wooden boxes and empty cans, built a bookcase for his small library; his leisure, what little there was of it, was spent in reading, drawing, photography. In due course he also succumbed to malaria and dysentery, complicated after a while by dropsy. In the course of his illness in Cuba he took advantage of his enforced inactivity to learn English.

Transferred to a still more pestilential district at San Isidro, Cajal tended 300 patients, himself a gaunt dysentery-racked and shivering specter, apparently forgotten by his superiors, left to perish in the steaming jungle. By 1875 he was so ill with acute malaria that he had to be discharged and sent home.

Back in Saragossa, Cajal followed his father's advice and returned to his study of anatomy and histology, preparing for the competitive examinations that led to professorships. He was appointed temporary assistant in anatomy at a salary of 1000 pesetas (less than $200) a year; two years later he became temporary auxiliary professor at the Faculty of Medicine. Wrote he autobiographically: "I aspired to be something, to emerge from the plane of mediocrity, and to collaborate, if my powers permitted, in the great work of scientific investigation that I hoped might bring some measure of glory to my sad country."

Microscopy. Ramón y Cajal's lifelong romance with the microscope began when for the first time he unearthed an ancient instrument in the physiology laboratory, was able to see blood circulating in the web tissue of a frog's leg. Out of what was left of his Cuban pay he bought an up-to-date Verick microscope for $140, payable in four installments.

Spanish medical circles were at that time indifferent to histology, if not openly hostile. There was no one to teach Cajal, forcing him to experiment by himself, using Louis Antoine Ranvier's textbook on histologic techniques translated from the French. During what he later called his "honeymoon" with the microscope, he examined everything he could: blood corpuscles, epithelial cells, muscle fibers, nerve fibers, drawing and photographing as he went along; he once spent twenty continuous hours at the microscope, enthralled by the mysterious progress of leukocytes through membranes and vessel walls.

This period of exploration was interrupted when he one day suddenly suffered a severe hemoptysis, followed some days later by another and more massive incident. The diagnosis of tuberculosis was not in doubt: high fever, dyspnea, hacking cough, copious perspiration. He became gloomily convinced that his short life would soon be ended, his career cut off before it began.

His father wasted no time on morbid thoughts, packed him off to the baths at Panticosa to lie in the sun and drink the waters, with his sister Paula to look after him. At first Cajal's despair was so profound that he several times considered leaping to his death from a crag.

In time he became tired of the monotonous sanatorium routine, decided that he was not going to die after all. He stopped taking the waters, threw away his medicines, ignored the prescription of diet and rest. Instead, he hiked around the countryside sketching and photographing, ate plenty of good meat, drank rich milk, basked in the sun. In a few months he was quite well again, returned to Saragossa.

Ramón y Cajal and students at the Laboratorio de Investigaciones Biológicas *where he laid the foundation of a school of Spanish histology.*

In 1879, Cajal sat for competitive examinations, obtained the post of director of anatomic museums in the Faculty of Medicine in Saragossa. In that year he married Silveria Fananás García; on his salary of about $30 a month this was considered by his father and his friends to be sheer folly. But he had chosen wisely: his wife did not waste money on the vanities of dress, on social entertainment and expensive furnishings; she devoted herself entirely to her husband's work, to their children, and to managing their modest home.

The outbreak in 1885 of a cholera epidemic which quickly spread from Valencia throughout Spain interrupted his histologic research; at the government's request he prepared a monograph on cholera in which he suggested that immunity might be produced by inoculation with a dead culture.

Nervous System. In his studies of the nervous system, begun in Barcelona in 1887, Cajal applied Italian anatomist Camillo Golgi's chrome-silver stain to embryonic brain tissue at a stage before its fine structure is obscured by the growth of the myelin sheath; he effectively isolated the previously unobserved basket cells, mossy fibers, peridendrite spines, climbing fibers, first in bird brains, then in small mammals.

His law of transmission of nervous impulses by a series of cells through contact opposed the then widely accepted reticular hypothesis of transmission through a continuous network of nerve fibers. He spent his small savings on publication of his views in his own journal, *Revista trimestral de histología normal y patológica*, 60 copies of which were distributed among scientists abroad.

After waiting a year for some notice to appear in scientific journals of his newly published research, he went to the Berlin meeting of the German Anatomic Society in the fall of 1889, presented an impressive histologic display that won over a former adherent of the reticular hypothesis, Swiss histologist Koelliker, and several other leading scientists.*

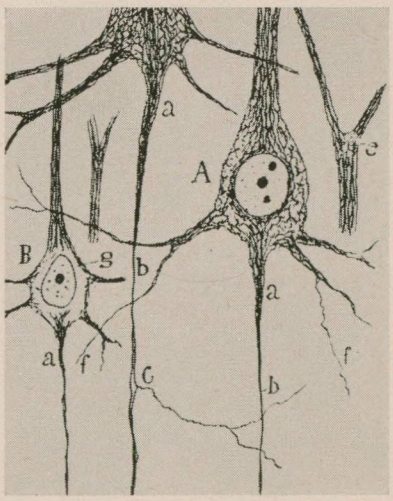
*Professor Waldeyer of Berlin who coined the term "neuron theory," still receives credit in many textbooks for Cajal's discoveries.

In rapid succession Cajal completed studies on impulse conduction summed up in his theory of dynamic polarization, propounded the neurotropic theory which became the basis of widespread research on the regeneration of nerve tissue, presented his report on the morphology of the nerve cell, in which he postulated for the first time the now accepted psychologic principle that intellectual power depends on the richness of the cerebral neurons' connective process instead of on their size and number.

Honors. An invitation to deliver the Croonian lecture before the Royal Society in London set off an avalanche of honors; the previous Croonian lecturer, Virchow, later asked a prominent Spanish academician in Berlin about Cajal's latest work, drew a blank look from his visitor, who hurried home to sponsor election to the Royal Academy in Madrid of the colleague whose name he first heard from the renowned German pathologist.

Outstanding in the growing cluster of awards were the Moscow Prize of 5000 francs at the 13th International Medical Congress in 1900 for the most significant contribution to medical science since the previous congress, the Nobel Prize shared in 1906, with Golgi.

Moved by published stories of Cajal's triumph over poverty and hardship, the government established in Madrid the Laboratorio de Investigaciones Biológicas, installed Cajal as director at an annual salary of 10,000 pesetas, which he insisted on reducing to 6000. The



Drawing of ganglia, left, by Ramón y Cajal; pyramidal cells of 10-day-old dog, above, were identified by the silver nitrate method.

laboratory became the center of the Spanish school of histologists, among them Nicolás Achúcaro, who developed a new stain for connective tissue; Pío del Río Hortega, discoverer of the microglia and oligodendroglia; Dr. J. F. Tello y Muñoz, his master's successor as director of the laboratory, later renamed the Instituto Cajal.* As research director and teacher he urged the youth to shake Spain out of the lethargy of centuries and advance it to the forefront of scientific achievement.

Interests. Ostensibly a recluse wrapped up in research and family life, Cajal during his years in Valencia organized a camera club for which he drafted a constitution prohibiting discussion of controversial subjects (acceptable topics: science, art, literature), set up a circle to investigate hypnotism.†

An avid chess player, he sacrificed this interest for the sake of research, confined his social activity to the evening hour at a favorite café. For diversion at home he bought one of the new Edison phonographs, modified the design to improve tone and volume, discovered on a visit to the United States in 1899 that his basic improvement had been introduced into the latest models.

Writings. At the peak of his productive powers, Cajal published 14 scientific articles in 1903, completed in his lifetime more than 200 scientific works, among them the textbooks *Manual of Normal Histology and Micrographic Technic* and *Manual of General Pathologic Anatomy*, the monumental three-volume *Texture of the Nervous System of Man and Other Vertebrates*, the classic work embodying several years of research, *Studies on the Degeneration and Regeneration of the Nervous System*.

Under the pen name Dr. Bacteria he wrote popular articles for the magazine *Ciencia*, reviving an interest of student days when under the influence of Jules Verne's *Voyage to the Moon* he had written a novel of adventures on the planet Jupiter by a bold earthling who sails through the circulatory system of mammoth creatures shaped like men. Wrote he: "I regret that I have lost this book, for it might have been transformed, in the light of the modern revelations of histology and bacteriology, into a delightful work of scientific popularization."

His literary and other nonscientific works include the vivid autobiography *Recuerdos de mi vida*, two volumes of pungent aphorisms culled from café talk *(Charlas de Café)*, *Vacation Tales* (including the macabre tale of a scientist who uses bacteriology to avenge marital infidelity), the *Psychology of Don Quixote and Quixotism*, a book on color photography. In the grand finale to his life and literary work, *The World as Seen at Eighty*, he recorded with clinical calm his sensations resulting from arteriosclerosis of the brain. He died in 1934, retaining his lucidity to the last moment.

The Man. From his rapscallion beginnings, Ramón y Cajal developed into a controlled personality, imposing self-discipline where no one had been able to impose it before. He was prodigiously industrious, working for long hours at a time at the microscope and the microtome. Said he: "The object of my work was, above all else, to give myself a lasting stimulus to creative work. Foreseeing the hours of discouragement and fatigue that lay ahead, I wished voluntarily to give up my liberty by making a pledge of honor to the public."

His career showed many contrasts and contradictions: he originally wanted to be an artist, he became a scientist; an ardent patriot, he took little part in his country's politics and never saw action in the field.

By nature he combined an expansive idealism with a sophisticated irony. At heart he was a profound pessimist and his craggy face in repose generally wore an expression of sadness. Yet for all his mordant wit, his colleagues not only admired him, they loved him, calling him affectionately Don Santiago. His students left innumerable tales of his kindness to them when they were in difficulties, of his encouragement when they were overwhelmed by problems.

As a teacher, he showed that he was a true scientist and not a pedagogue by refusing to exert pressure on his pupils, or influencing them with his ideas to interpret the results of their own research. Said he: "The ideal of science is to elucidate the dark mysteries and unknown forces which invest us, for the benefit of our descendants and to make the world more agreeable and intelligible, while we ourselves are forgotten, like the seed in the furrow."

Estimates. Wrote Dr. James J. Walsh in 1901: "Ramón y Cajal's demonstration of the role in brain structure and function of nerve cells whose prolongations contract under irritation, created the scientific foundation for understanding loss of consciousness through fatigue or shock, acquisition of facility through exercise of the brain cells, mnemonic failure, other psychic phenomena."

Observed Drs. August and Jaime Pi-Suñer that, like Renaissance anatomists, Cajal endeavored to explain physiology by anatomy, with uneven results. Noted they that his suggestions regarding interruption of current through synapses and the isolating action of neuroglia have been definitively refuted.

Declared Dr. Gregorio Marañón before the Royal Academy of Medicine in Madrid in 1950: "We are conscious of the abyss which separates a book on neurology written before 1880 and one written today; the contrast between a treatise on psychiatry published in the last decade of the 19th century and one published today is even greater. The progress which has been made is due in great part to Cajal. Cajal, Sherrington and Pavlov are the three men who have done most to provide a rational explanation for the mystery of the nervous system."*

Summing Up. In the words of Cajal: "I have aimed that my life should be, as far as possible, a living poem of intense action and secret heroism in the cause of science." END

*Earnest foreign disciple, who studied at the Institute after Cajal's retirement, was Wilder Penfield, later director of the Montreal Neurological Institute.

†He acquired such fame as a "healer" that his house became a shrine for all kinds of strange patients.

*Stamps were struck for him, numerous buildings and institutions were named after him.

Monument to Ramón y Cajal, Parque del Retiro, Madrid, by Victorio Macho showing a reclining effigy in the classic style.