

Section of Pathology

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Santiago Ramón y Cajal (1852-1934)

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THE scientist whose centenary we commemorate this year will be remembered not only as the greatest of neuro-anatomists, but also as a writer of distinction, a pathologist, a philosopher and a patriot. He secured for Spain a place of honour in a rapidly expanding world of medicine, establishing a school of histology which revolutionized the methods of approach to the problems of neuro-anatomy, and influenced the contemporary worlds of physiology and neuropathology. Civil war hastened the dissemination of his teachings, for many of his pupils scattered over the world to add their important quota to biology.

Cajal's father, Ramón, a resolute and energetic man, had had to content himself with the life of a non-qualified surgeon until such time as he could afford to complete his academic career: this he did when Santiago, the eldest of his five children, was already 6. Cajal's mother was a robust highlander who had known her husband since childhood.

The family left the isolated and impoverished village of Petilla in Aragon when Santiago was 2 years old, and two years later he went to school. His father, a profound believer in the sovereign will, also taught his little son, and the two would retire to the abandoned cave of a shepherd to avoid interruptions. At the age of 6 the bashful but intelligent Santiago became the amanuensis of the household and his father's secretary.

With a domineering and exacting father one understands why Cajal as a boy was wayward and secretive. A shy aloofness, in fact, dogged him throughout life. But he had a great respect for and fear of his sire. In fact he claimed to owe everything to the traits of character which he inherited from him.

When he was 8 the family moved to Ayerbe, where Santiago, who shunned the society of others, preferring to walk alone in order to enjoy the landscape and the flight of the birds, was mocked by the boys of the town. To this persecution he reacted by excelling them all in their diversions of stone throwing, pillage and robbery. Parental floggings, beginning with a whip and ending with cudgels and tongs, would inspire terror in him and his younger brother, a faithful partner in many a daring escapade. One wonders if Santiago's over-compensation had its origin in his father's endeavours to strangle a passion for sketching which was now beginning to assert itself. Ramón senior had no use for art so Santiago found it necessary to draw and colour in secret. At school he had an unenviable reputation for obstinacy and paid many visits to the mouse-infested dungeon where he discovered for himself the principle of the camera lucida.

At the age of 10 he was sent to the Scola Pia (Escolapios) at Jaca, but he was indolent and inattentive. In vain, he tells us, the energetic exhortations of Father Jacinto, who with furious blows from the strap and cat-o'-nine-tails made his case a matter of personal pride, failed to recall him to reality. "The blows sounded in my head", he wrote, "like those of the door knocker in an empty house." The disciplinary fasts and the repeated beatings upset his health and he was taken home. While convalescing under his mother's care he made gunpowder and a cannon, the first

discharge of which demolished a neighbour's gate and landed this student of ballistics in the town jail. The incident shows, I think, that he had acquired a facility for analysis and synthesis at an early age.

At the Institute of Huesca, where he is honoured as a past student, he continued his schooling, but a liking for the sport of Mars still pursued him. In his third year there he was able to report: "My ability with my fists and my skill in the use of the sling and the cudgel inspired respect in the bullies of the upper years." One day when pretending to work in his father's pigeon house, he found his way on to the roof of an adjoining confectioner and lo—on looking into an open garret window saw a library of books and a tempting display of candied fruits. With commendable judgment he avoided the sweetmeats but the volumes he proceeded to devour surreptitiously one by one. It was *Robinson Crusoe* which appealed to him most: "what a supreme triumph it must be to explore a virgin territory, to gaze upon scenes untouched by the hand of man . . . which seem created expressly for the discoverer as a reward for his outstanding heroism."

His father was worried. The uncontrolled imagination, the diletantism and the bellicose tendencies of his first-born were not calculated to make him into a man of professional standing. He, therefore, apprenticed him to a barber, as he himself had been, so that, should all else fail, he would have a trade in his hands. And so the awkward and stubborn Santiago, with a longing to explore some primordial jungle, came to acquire skill with the razor. Next he was sent to a coarse and ruthless shoemaker of evil countenance who agreed to tame and harness his apprentice. But the vivid imagination of the introvert always took charge of a situation. "Whenever I had finished supper", he wrote, "I eagerly hastened to my little room and until I fell asleep spent my time giving form and life to the jumble of stains on the wall and the cobwebs of the ceiling which I transformed . . . into the wings of a magic stage, across which filed the cavalcade of my fantasies."

His martial ambitions received a setback when, as a boy, he witnessed the battle of Linas de Marcuella. The cries and groans of the wounded and the intensely white face of the dying general propped up on his horse taught him the terrible lesson of death. "What distressing indifference is that of nature", he wrote, "as it casts away . . . the masterpiece of creation, the sublime cerebral mirror, in which it acquires consciousness of itself." Fear would often grip the youth, in spite of his bravado. When he made his first train journey he panicked at the sight of the engine—"a hideous fire-belching mass of metal and coal . . . my alarm increased as I observed the disproportion between the size of the locomotive and the flimsy, rusty and disconnected rails, further weakened by rivets. . ." Paralysed with terror he refused to board the train but his colossal grandfather forced him into a carriage. An unusual reaction for a boy of 14, I think. Which of us at this age would be critical of the permanent way?

By now his father saw promise in his shoemaker son, so decided to interest him in osteology. He wanted to make him a surgeon rather than a physician "for", he said, "man bows only before crimson glory: a little blood heightens the splendour of the success, stamping it with the hall-mark of popularity." Together they climbed the walls of a cemetery by moonlight picking out from the shoal of bones half buried in gravel and nettles those which were most perfect. Although safe with his father fear laid hold of him: "I seemed to hear in the rattling of the bones protests . . . from the defunct."

The sullen Santiago, proficient now with razor and needle, was entered as a student at Zaragoza. About the same time his father was appointed a temporary professor of dissection. Father and son worked devotedly together. "There is no teacher more zealous than he who studies in order to instruct", wrote Cajal. But he still retained a passion for gymnastics, and for the sake of a comely young woman with blue eyes, with whom he was scarcely acquainted, he wellnigh choked a rival. Likening an athlete to a country with a large standing army he believed that excessive muscular development must lead inevitably to violence and bullying. One would have to be an angel, he wrote, to restrain in continual inactivity hypertrophic muscle fibres anxious for employment and justification. He absorbed the French romanticists and the thrills of Jules Verne. In fact he wrote the adventures of a microbe sailing on a red corpuscle to watch the epic struggles between leucocytes and parasites. Later this little germ found its way to the brain and discovered the secret of thought and of the voluntary impulse. How prophetic! Here was the desert island waiting for *Robinson Cajal*!

He saw army service in Cuba, showing promise as an administrator; but malaria and dysentery ruined his health and on his return from what proved to be a costly and futile campaign he saw many of his fellow patriots buried at sea. His cachexia and jaundice also lost him his betrothed and soon, to add to his misfortunes, he had a hæmoptysis, which needed all his father's skill and understanding to rectify. His disease must have been serious for he was dyspnoëic, emaciated and profoundly depressed. He wrote of his convalescence: "one afternoon, seized with a fit of gloomy melancholy I scaled a lofty crest which I reached breathless and fainting . . . I conceived the plan of letting myself die with my face to the stars, far from men and with no witnesses other than the eagles nor shroud other than the approaching snows of autumn."

The sun, silence and art were his physicians and in fifteen months he was ready and eager to work for the regeneration of his country. His tool would be the microscope. Against the advice of his family and a priest the timid Santiago married a green-eyed golden-haired girl with "an air of

child-like innocence and melancholy resignation", after first satisfying himself that her psychological make-up was the complement of his own. From her he expected and received "soft obedience": to her he was always gallant and attentive.

In an attic which he equipped as a laboratory he spent what he called his honeymoon with his Verick microscope. He bought a simple Ranvier microtome and periodicals, mostly in French for he knew no German. In 1880 he wrote his first paper on inflammation in the mesentery, cornea and cartilage, illustrating it with his own lithographs. This prodigious worker wrote during his scientific lifetime 287 other monographs and papers besides 15 textbooks. Well has Dr. Courville called him the "Hercules of Histology". Referring to one strenuous bout of authorship Cajal said: "It was a delicious rapture, an irresistible enchantment." His reclusion now stood him in good stead. "Solitude creates for ourselves", he wrote, "the illusion of complete freedom."

An epidemic of cholera, which called for his help, almost tempted him into the exciting science of bacteriology, but he abandoned it on the grounds of economy. It required a whole Noah's Ark of propitiatory victims, he found, as well as a series of expensive gas incubators. He wrote: "I finally chose the cautious path of histology, the way of tranquil enjoyment. I knew well that I should never be able to drive through such a narrow path in a luxurious carriage." His devoted wife, with the care of a family which eventually increased to six, agreed to a proportion of his modest income being diverted for the purchase of glassware, reagents and periodicals, and even to the publication of a quarterly review.

From Zaragoza he moved to Valencia, Barcelona and finally to Madrid. Success accompanied him throughout and honours showered in upon him, not always to his liking, for, as he said: "Fame bruises while it caresses: it kisses, but it crushes." He became a national hero and was even offered a ministry of cabinet rank.

It was Don Luis Simarro, the psychiatrist of Valencia who, in 1887, demonstrated to Cajal in Madrid the methods of Golgi and Weigert-Pal. He could not sleep that night for excitement, for until then he had had to content himself with the cruder tinctorial methods in vogue or to make use of microdissection, not, however, without its fascination for the pupil of Robinson Crusoe. "What a triumph it was to clean from its neuroglial bramble thicket a cortical pyramid, that is the noble and enigmatic cell of thought."

In Valencia he worked in the post-mortem room classifying tumours and studying tissue reactions around them. He spent some of his happiest days in this city with congenial company at the cafés, which, however, it seems he attended more for self-discipline than choice. "It was necessary", he wrote, "to allot to each cell its rations and to each reasonable instinct a convenient opportunity for exercise." On Sundays he walked among the palms and the pines of the coast enjoying the *arroz* in the company of friends. Photography, chess and hypnotism were for a time his diversions.

1888 was his year of fortune. Working with embryonic material and with the aid of the procedure of double impregnation he was able to show that an axon could, by means of collateral and terminal branches, make contact with a variety of neurones. Later he deduced that the cell bodies and their processes took part in the chain of conduction, postulating the law of Dynamic Polarization, in which he generously gave part credit to Van Gehuchten. He rejected Gerlach's conception of the anastomotic network of nerve processes, an hypothesis defended by Meynert and Golgi and practically all neurologists. Instead he supported the "free ending" theory which had been advanced by His and by Forel. But transcendental problems faced him at each discovery. "What mysterious forces", he wrote, "precede the appearance of the nerve processes, promote their growth and ramifications, stimulate the corresponding migration of the cells and fibres in predetermined directions, as if in obedience to a skilfully arranged architectural plan, and finally establish those protoplasmic kisses, the intercellular articulations, which seem to constitute the final ecstasy of an epic love story?"

In the year 1903 he studied the neurofibrils; as the then-existing techniques of Bethe and Apáthy were inadequate he set his subconscious mind to work on the problem. The answer came to him in a flash as he was returning from a holiday in Italy: why not use hot silver nitrate? So preoccupied was he with his plans that he failed to enjoy the beautiful riviera scenery, but back in Madrid he "fell upon" his animals and his efforts were crowned with success.

In 1889 he journeyed to Berlin with his microscope and, speaking in French, demonstrated his preparations before the illustrious members of the Anatomical Society. The prejudice which he anticipated because he was a Spaniard did not materialize. Spain, he knew, had been known for artists, long-haired poets and gesticulating dancers, but not for scientists. He was well received, and Von Kölliker, who had visited Golgi two years earlier, now abandoned the reticular theory and went so far as to learn Spanish in order to read Cajal's earlier communications. He had many good friends in Germany. To Krause of Göttingen he owed his introduction into the scientific world, for his worthy published articles for him, paying for the chromolithographs himself; while to a chance recommendation of Virchow he owed his membership of the National Academy of Sciences in Madrid. On his way to Berlin Cajal called on Weigert, Etinger and Ehrlich and on his way back on his patron Krause, and Golgi: the latter, however, was not in Pavia but in Rome where his duties as

a senator had called him. Cajal met Golgi in Stockholm when they shared the Nobel Prize in 1906: he was at the station along with many others to meet the eminent Italian, his senior by nine years, but the friendliness which he had cause to expect was not forthcoming. Cajal, who was always punctilious in acknowledging his debt to the technique of his "illustrious colleague Golgi", had been accused by Golgi of not having given him credit for the discovery of the collaterals in the spinal cord. But he had published in an obscure provincial journal and it was not Cajal's fault that it was unknown to the world. At Stockholm Golgi chose to resurrect the defunct network theory and in so doing "made a display of pride and self-worship so immoderate that they produced a deplorable effect on the assembly." Cajal, who believed that the unsheathed sword in debate should be tipped with a bouquet of roses, says: "I was trembling with impatience as I saw that the most elementary respect for the conventions prevented me from offering a suitable and clear correction of so many odious errors and so many deliberate omissions." Separated in life they have been united in death—for they figure side by side on a medal recently struck in their honour.

Cajal was ill-at-ease in Stockholm; for prizes of this order, which cost him four months of his time in dealing with felicitations and follow-up ceremonies, one required, he said, "a heart of steel, the skin of an elephant and the stomach of a vulture." We can imagine the embarrassment of this diffident patriot when he learnt that the Prize for Peace was to be bestowed on Theodore Roosevelt. Cajal had, on the advice of his government, his friends and the Press, visited the United States only a few months after the war with Spain to take part in university celebrations at Worcester, Massachusetts. In America he disliked the women reporters. He did not really like women: like savages they suffered from an undue readiness to burst out laughing and in Southern climes they grew old too soon. Moreover, they wasted the precious time of the man of science, but he conceded that they were necessary. The wife, he said, is like the pack in battle—you can fight better without it, but what happens after the battle? He advised scientists to marry and to face up to the responsibilities of family life: the surest way to get women out of your mind, he argued, is to marry one of them. But he warned that only between the ages of 15 and 18 could a woman experience the emotion of real love, for only then is she free from ambition. The misfortunes of marriage, he held, had their origin in the fact that the woman does not choose but is chosen.

He visited England in 1894 in order to deliver the Croonian Lecture and stayed with the Sherringtons. The story is well known of how he locked his bedroom door so that the maidservant might not disturb the display of histological preparations which he had brought with him. It is said that his habit of airing his mattress from an upstairs window told the neighbours that a celebrity of unusual calibre was staying with the physiologist from St. Thomas's! Sherrington's description of him reveals a modest and simple man who in some respects was unusually naïve. He predicted the ultimate downfall of this country because of lack of industries, but his knowledge of England at that time was confined to what he could see from the continental boat train. At the Royal Society, presided over on this occasion by Sir John Lubbock, he was very nervous but was deeply moved when he saw the intertwined flags of Britain and Spain. He visited Oxford and Cambridge and returned to Madrid envious of our beautiful university cities.

But in Madrid he was happy; there he had friends in the *tertulia* of the Suizo café, and there he could walk on the banks of the Manzanares or in the parks where he would converse with acquaintances in humbler walks of life. But he closed his ears to the sound of the Siren of the capital. How easy was it for the bee to become a butterfly or even a drone! There was so much work to be done—the retina, both of man and insect, the synapses, the neuroglia and the comparative anatomy of the optic tracts, all craved his time. "My attention", he wrote, "hunted in the flower garden of the gray matter cells with delicate and elegant forms, the mysterious butterflies of the soul, the beating of whose wings may some day, who knows, clarify the secret of mental life."

He was of the sort who invites kindnesses. The Professor of Obstetrics gave his salary for the upkeep of the laboratory of which they were all so proud; the Professor of Surgery offered him a house, which it was not convenient for him to take. They made him Director of the National Institute of Hygiene and Biological Research, but the salary was reduced at his own request.

Short in stature and tending to stoop, he possessed broad shoulders and long arms. "His eyes were full and dark", said Sherrington, "lit or gloomed according to each mood." Cajal, this gifted and serious man, possessed, I think, all of what he styled the indispensable attributes of the researcher, namely mental independence, intellectual curiosity, perseverance, devotion to country and a desire for reputation. "'Tis from the sense you will find that knowledge comes", wrote Lucretius. Cajal was his own prosecutor rather than his own attorney.

He did not drink and did not smoke. In politics he was a democrat which suited, as he himself observed, his exaggerated individualism and his dislike for the principle of authority. The discipline of religion, however, he valued, "for", he said, "faith develops and leads to enjoyable longevity while doubt leads to pain in the soul and premature old age". The scientist, he held, as he contemplated the problems of Nature came near to the ideal of Henry James, of becoming a collaborator with God.

The aphorisms in his book *Charlas de café* reveal him as a cynic and pessimist imbued with a strong sense of justice and duty. He welcomed I think the principle of "the earth for all, talent for all" but

in 1910 he wrote: "will not the *aura mediocritas*, to which society aspires, enervate the mental faculties undermining the energy for scientific investigation? Will not collective capital be timid . . .? Will glory, the passion of philosophic and scientific genius, prosper in the grey and subdued atmosphere of the common weal?" But a time would come, he divined, when science would illumine the conscience and elevate the mind.

The First World War disheartened him. His dear friend, Van Gehuchten, had lost everything in the sacking of Louvain and was a refugee in England. He lost contact with all his colleagues abroad and felt isolated. "But", he said, "let us repel sadness, which is the mother of inaction: let us devote ourselves to life, which is energy, renovation and progress, and keep on working." "It is important", he wrote, "to put to use all our lucid moments, be it in meditation, which follows prolonged rest, or in the superintensive mental work which only the nerve cell heated by congestion can produce, or finally, in unforeseen intuition which frequently flies out, like a spark of steel, from the impact of scientific discussion."

Cajal was a kindly and inspiring teacher but he could be obstinate and even defiant. Once when a student threw orange peel he turned round from the blackboard and angrily offered to meet the culprit for a settlement outside the university precincts: at this time he would be close on 60. The sensitive and modest del Rio Hortega, whom it was my privilege to know, revered him like a father. In fact one saw the master mirrored in the pupil. They had the same diffidence, the same artistic and poetic sense, and in the formal gardens and intricate forests of the brain they satisfied their love of form and beauty and their thirst for adventure. Superb technicians, prodigious workers and lovers of Spanish culture, they had so much in common: Cajal influenced throughout life by his father; Hortega influenced by Cajal, although not of Cajal's wishing for he warned his pupils against extreme admiration of one's teacher. "It drains the personality and clouds the understanding", he said. An intriguing porter, resentful because the administrative strictness of Hortega had deprived him of certain perquisites, made trouble between them, misquoting to Cajal the words of Hortega in his lectures to students. Cajal, furious and insulting, ordered his junior to quit the Institute. Poor Don Pio, deeply wounded and weeping, did so. He did not return for several years until Cajal, acknowledging his own error in a happy way, invited his faithful assistant to demonstrate his excellent preparations. Don Pio imagined, I seem to recall, that his chief was a little jealous of his successful analysis of "the third element" of the brain.

Dr. Wilder Penfield and Don Pio on their last visit together found Don Santiago with a cold, propped up in bed surrounded by manuscripts. "Deafness and feebleness which had come on him recently were shutting doors behind him and the world, but his eyes blazed under shaggy brows showing an unquenched fire." He died peacefully in his eighty-third year while the great Cajal Institute on the hillside was under construction, a solid symbol of the renaissance of science in Spain.

"Cajal", wrote Sherrington, "reshaped our knowledge of the cellular architecture of the nervous system. He had, it is true, pulled down much, but he had built up more." For him the horizon of histology was limitless and all might share in the work and the satisfaction it gives. He wrote: "There await in the bosom of the living being millions of palpitating cells which, for the surrender of their secret and with it the halo of fame, demand only a clear and persistent intelligence to contemplate, admire and understand them." "Science so far from being exhausted, invites everyone with inexhaustible veins of ore." And for Britons he had a special word of encouragement for, he said, "grey matter goes with grey skies."

BIBLIOGRAPHY

- CANNON, D. F. (1949) *Explorer of the Human Brain*. New York.
- CASTRO, F. de (1952) *Santiago Ramón y Cajal 1852-1934*. Primo Congresso Internazionale de Istopatologia del Sistema Nervoso. Rome.
- COURVILLE, C. B. (1952) *Bull. Los Angeles neurol. Soc.*, 17, 1.
- DOLC, M. (1952) *Ramón y Cajal en el Instituto de Huesca*. Huesca.
- GARRISON, F. H. (1929) *Bull. N.Y. Acad. Med.*, 5, 483.
- GIBSON, W. C. (1936) *Ann. med. Hist.*, 8, 385.
- LAFORA, G. R. (1935) *Tierra Firme*, 1, 31.
- (1952a) *Homenaje a Ramón y Cajal*. III Congreso Nacional de Neuropsiquiatria, Asociacion Espanola de Neuropsiquiatria, p. 15.
- (1952b) *Cajal en su total Humanidad*. *Foco*, No. 7, p. 5.
- LLURIA, E. (1910) *Super-organic Evolution* (Preface by S. Ramón y Cajal). London.
- LOCATELLI, P. (1926) *Arch. Neurol. Psychiat.*, Chicago, 16, 213.
- (1951) *Sci. med. ital.*, 2, 375.
- PENFIELD, W. (1935) *Arch. Neurol. Psychiat.*, Chicago, 33, 172.
- RAMÓN Y CAJAL, S. (1937) *Recollections of my life*. Trans. by E. Horne Craigie. Philadelphia.
- (1951) *Precepts and Counsels on Scientific Investigations*. Trans. by J. M. Sanchez-Perez and edited by C. B. Courville. Mountain View, Calif.
- SANCHEZ-PEREZ, J. M. (1952) *Bull. Los Angeles neurol. Soc.*, 17, 47.
- SHERRINGTON, C. S. (1934) *Nature, Lond.*, 133, 871.
- (1935) *Santiago Ramón y Cajal*. Obituary Notices of Fellows of the Royal Society. London, 1, 424.
- SPRONG, W. (1935) *Arch. Neurol. Psychiat.*, Chicago, 33, 156.